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## ERRATA

Vol. 43 No. 4 p. 344 in first and second lines of summary of paper by ALVES & BLAIR the reference should read [this *Bulletin* 1945 v. 42, 815]

Vol. 43 No. 5 p. 412 ZUCKERMAN's title should read "In vitro opsonic tests with *Plasmodium gallinaceum* etc."

Vol. 43 No. 5 p. 449 in second line of summary of paper by MOVTEL, for 951 read 851

In the abstract of SCHLOSSER's paper on *W. bancrofti* infection in the Solomon Islands area, this *Bulletin* 1946 v. 43 575 the mosquitoes *Anopheles punctulatus punctulatus* and *Anopheles punctulatus farauti* used in feeding experiments with microfilariae were incorrectly referred to as *Aedes*.

In the abstract of the paper by GRASSET, SCHAAPEMA and HODGSON this *Bulletin* 1946 v. 43 671 line 2, the dose of venom of *Hadogenes*, needed to kill a guinea pig, when injected subcutaneously is given as 185 gm. This should read 185 mgm.—ED

# TROPICAL DISEASES BULLETIN.

Vol. 43]

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## SUMMARY OF RECENT ABSTRACTS \*

### I CHOLERA

#### *Epidemiology*

ROGERS (p 282) has collected additional data from India which support the contention he has previously made that epidemics of cholera can be forecast by close observation of the south west monsoon rains of July to October. The danger of spread of cholera by pilgrims returning from a fair can be foreseen from the climatic data at the time and a knowledge that cholera is present in the areas through which the pilgrims have to travel. Rogers concludes that as the climatic conditions are beyond human control the only means of prevention is by protective vaccination. In the discussion which followed the reading of Rogers's paper a speaker expressed doubt as to the value of vaccination in previous years but thought that the vaccine now available is probably better than that previously used. Cholera however is amenable to improvements in environmental domestic and personal sanitation.

In discussing the epidemiology of cholera in the Punjab YACOB (p 119) notes that the most recent fair held at Thanesar in 1941 passed off without a single case although it was attended by 500 000 pilgrims. This appears to be evidence of the efficiency of the Punjab health organization but the author seems to think that for other pilgrim centres protective inoculation of all pilgrims is the only means that can be expected to control the epidemics.

In the Kunming epidemic of 1942 93 per cent of the vibrio strains isolated were of Inaba type 7 per cent. of Ogawa type (TANG *et al* p 120)

#### *Aetiology*

In a detailed study of the growth conditions of *V. cholerae* LINTON and JENNINGS (pp 377-78) describe a simple casein digest medium to which certain salts and glucose are added and through which air (with a proportion of CO<sub>2</sub>) is continuously bubbled. In this medium (for details of which the original abstract should be consulted) when the concentration of glucose is at the optimum (1 per cent.) the vibrios grow well to yield a five-fold increase over previous methods and as the pH is regulated by the aeration are not destroyed by the acid formed as a result of fermentation of glucose. Cultures in this

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945 v 42. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

MOORE L. D. Incidence of Malaria among Troops in Liberia. *J. National Malaria Soc.* Tallahassee Fla. 1945 June v 4 No 2 109-13

The first contingent of U.S. troops arrived in Liberia in June 1942. Coloured troops outnumbered white by five to one. They were stationed in a highly malarious area. *Anopheles gambiae* was very prevalent. Between 80 and 90 per cent. of the indigenous infants harboured parasites, all *Plasmodium falciparum* and half of these infants harboured gametocytes. The first echelon was replaced by a second in March 1943 when the ratio of black to white troops decreased to three to one.

The first echelon was given suppressive quinine for the first five months of their stay between 50 and 75 per cent. took it regularly 40 grains a week. The incidence of malaria was 38.8 per cent. initial attacks 16.0 per cent. subsequent attacks a total of 54.8 per cent. attacks of malaria during a period of 8 months.

The second echelon lived under much better sanitary conditions but received no suppressive treatment for the first four months after arrival. They had much higher malaria rates. For a six month period the initial attack rate was 86.3 per cent. subsequent attacks 58.1 per cent. or a total malaria attack rate of 144.4 per cent.

Norman White

DAS GUPTA, B. M. & SIDDOXS, L. B. The Parasitology of Malaria among Destitutes in Calcutta during and after the Bengal Famine of 1943. *Indian Med. Gaz.* 1945 Mar v 80 No. 3 160-64 4 figs.

During the disastrous famine in Bengal in 1943 large numbers of destitute persons found their way to Calcutta mainly from the neighbouring districts 24 Parganas Hooghly and Midnapur. Between September 1943 and December 1944 the blood of 14,862 of these destitutes was examined. Malaria parasites were found in 4,920 (33.1 per cent.). The maximum incidence occurred in December 1943 44.0 per cent. and in November 1944 51.7 per cent. *P. falciparum* was responsible for 48.8 per cent. of the infections *P. vivax* 49.7 and *P. malariae* for only 1.4 per cent. This incidence of *P. malariae* infections is unusually low for Bengal it usually amounts to 12 per cent. or more. *P. vivax* on the other hand was more in evidence than is usual in Bengal. The minimum malaria incidence was in June two months later than normal. The *P. vivax* curve was unusual it rose steadily from November 1943 to August 1944 4 or 5 months later than the normal peak. The *P. falciparum* curve corresponded closely to that of total malaria. The undue prevalence of *P. vivax* may have been due in part to more frequent relapses than normally occur among the indigenous population malnutrition and inadequate treatment occasioned by the shortage of antimalarial drugs may have been responsible for this.

Norman White

BRUMPT E. Anophélisme sans paludisme et régression spontanée du paludisme [Anophelism without Malaria and Spontaneous Regression of Malaria.] *Ann. Parasit. Humains et Comparés.* 1944-45 v 20 No 1-2, 67-91 [Numerous refs.]

This interesting dissertation is concerned with the large amount of work that has been done to explain the phenomena of anophelism without malaria and the spontaneous disappearance or diminution of malaria incidence more especially in temperate areas of Europe. A critical study of this kind does not lend itself to summary but some of its conclusions can be briefly stated.

Malaria in certain areas of Europe has often disappeared without any material alteration of conditions of housing of agricultural methods of conditions of

life generally and in spite of the persistence of numerous anophelines. In other areas malaria has disappeared as a result of a change in agricultural methods the elimination of saline surface water and the diminution of mosquito breeding places. Such methods have failed in other places where certain species of *Anopheles* or biotypes (*labranchiae clutus*) have been present. In places where malaria has disappeared and in which the abundant *A. maculipennis* present are biotypes that are but little attracted by man the regression has often begun by a diminution in the number of gamete carriers in part attributable to the use of quinine. In some such places malaria has reappeared when fresh gamete carriers have been introduced in the population. Numerous cases of locally acquired malaria in areas which had been long free from the malaria which formerly afflicted them have been reported in France and else where during the two great wars some in the neighbourhood of prisoner of war camps.

Norman White

YOUNG M D STUBBS T H MOORE J A EHRLMAN F C HARDMAN N F  
ELLIS J M & BURGESS R W Studies on Imported Malarias 1 Ability  
of Domestic Mosquitoes to transmit *virax* Malaria of Foreign Origin J  
National Malaria Soc Tallahassee Fla. 1945 June v 4 No 2, 127-31

In Columbia S C San Francisco and Longview Texas special laboratories have been collaborating in an experiment to determine the capacity of American vector species (*Anopheles quadrimaculatus* Say and *Anopheles maculipennis freeborni* Aitken) to transmit strains of *P. vivax* imported from overseas.

One hundred and sixty lots of mosquitoes were fed on 151 patients suffering from relapsing *P. vivax* malaria. The probable origin of the infections studied was Guadalcanal 96 New Guinea 33 other South Pacific areas 7 Mediterranean area 18 (Africa 9 Europe 9) and Trinidad 6. The percentage of lots infected according to origin of infection was Pacific area 68 Mediterranean area 67 South America 67. Among the infected lots the total number of infected *A. quadrimaculatus* was 959 out of 2,489 dissected or 38.5 per cent. Infected *A. freeborni* numbered 1,358 out of 2,581 dissected or 52.6 per cent.

Infected mosquitoes were applied to neurosyphilitic patients. From 32 imported malaria cases transmission to 59 white patients was attempted. 21 of the strains produced infections in 43 patients.

The conclusion is that imported strains of *P. vivax* malaria can be spread by local species of *Anopheles* in the United States just as readily as indigenous strains of malaria.

Norman White

CHWATT L J The Morphology of the Pharyngeal Armature in *Anopheles gambiae* and *Anopheles gambiae* var *melas* from Southern Nigeria. *Ann Trop Med & Parasit* 1945 Oct. 10 v 39 No 2 124-8 3 figs. [12 refs.]

Attempts to separate *Anopheles gambiae* type form from its variety *melas* (raised to specific rank by RIBBANDS in 1944) [this *Bulletin* 1945 v 42 3] are still a matter of considerable uncertainty. Of all the characters and methods of differentiation so far tested the least unsatisfactory is based on the structure of the egg.

Material from Lagos identified in this way as containing thirty five *A. gambiae* and twenty five *A. gambiae* var *melas* was prepared for microscopic examination of the bucco-pharyngeal armatures. Comparison showed that there are no determinable and consistent differences between the two forms and that individual variations are extremely small. A full description of the bucco-pharyngeal armature of *A. gambiae* is given and illustrated. [See also this *Bulletin* 1945 v 42, 860]

H S Lesson



STONE A. Some Relationships of *Anopheles lungae* Belkin and Schlosser (Diptera: Culicidae). *J. Wash. Acad. Sci.* 1944 Aug 15 v 34 No. 8 273

*Anopheles lungae* Belkin and Schlosser is closely related to *A. tessellatus* Theo. and to *A. longirostris* Brug. Characters are given for separating the females. The larva of *A. lungae* is distinguishable from that of *A. tessellatus* but as yet no differences from that of *A. longirostris* have been observed.

The three species have characters in common which distinguish their adults and larvae from those of *A. punctulatus* Dön., *A. annulipes* Walker, *A. farauti* Lav. and *A. amictus* Edw.

*A. tessellatus* occurs from India to Hong Kong, in the Netherlands Indies and the Philippines, with a few records from the Moluccas and a doubtful one from New Guinea. *A. longirostris* has been taken from New Guinea and New Ireland. *A. lungae* is confined to the Solomons. The distribution of these three species is not known to overlap. H. S. Leeson

OWEN W. B. A New Anopheline from the Solomon Islands with Notes on its Biology. *J. Parasitology* 1945 Aug v 31 No. 4 236-40 2 pls.

The female, male and larva (but not the egg or the pupa) of a new species *Anopheles kolensis* are described from material collected along the north coast of Guadalcanal in the Solomon Islands. The description is based on fifty caught females and their 500 progeny (300 females and 200 males) and several hundred other specimens. Of 500 females caught in tents over several weeks 90 per cent. were *kolensis*, 5.8 per cent. were *farauti* and 4.2 per cent. were *punctulatus*. During the same period 10 per cent. of the total anopheline larvae collected were *kolensis*, indicating that the new species has a greater preference for entering human habitations than the other anophelines, and thus is of primary importance in disease transmission.

Morphologically *kolensis* lies between *A. punctulatus* and *A. farauti* and the distinguishing characteristics are discussed. Adult and larval features of the new species are illustrated.

[Because of the obscurity of the taxonomic relationships of the *punctulatus* group it remains to be seen whether *kolensis* and *moluccensis* are identical. In this important complex group the following "species" have now been *A. punctulatus moluccensis farauti kolensis*.] H. S. Leeson.

BELKIN J. \ KNIGHT K. L. & ROZEBOOM L. E. Anopheline Mosquitoes of the Solomon Islands and New Hebrides. *J. Parasitology* 1945 Aug v 31 No. 4 241-65 27 figs. on 3 pls.

The anophelines dealt with in this paper are *Bironella* (*Brugella*) *hollandi* Taylor, *Anopheles* (*Miscomyia*) *solomonis* n. sp., *A.* (*M.*) *lungae* Belkin and Schlosser, *A.* (*M.*) *punctulatus* Doenitz, *A.* (*M.*) *farauti* Laveran and *A.* (*M.*) *kolensis* Owen.

Keys to the identification of females, males, pupae and fourth-stage larvae are given, but the authors consider that the key to the males is not entirely satisfactory. Detailed descriptions follow the keys, though the only egg described is that of *B. hollandi*. Taxonomy, distribution and biology of each species are discussed.

The new species *A. solomonis* appears to be closely related to *A. lungae*. Both occur in Guadalcanal; the latter occurs also in New Georgia and Bougainville and the former (doubtfully) in New Georgia. Larvae and pupae of both species have the habit of working their way out of the water on to leaves and banks, and they cannot be distinguished in the field. Little is known of the

habits of *A. solomonis* adults but *A. lungae* rests by day on tree trunks in swampy jungle two or three hundreds have been collected from one tree. They do not attempt to bite when disturbed but return immediately to their resting place. Activity begins about 6.30 p.m. and in an hour all adults are on the wing. About 6.30 a.m. they have all settled down again. In the Lunga area of Guadalcanal *A. lungae* formed about 2 per cent. of the total night catches for over a year the remainder being *A. farauti*. No *A. lungae* were taken in native villages and other evidence confirms that this species is not attracted to man.

*A. punctulatus*, *A. farauti*, *A. kolensis* and *A. moluccensis* form a closely related series in the group *Neomyzomyia* though the exact relationship of *moluccensis* to *farauti* and *kolensis* is not clear.

[In 1944 KNIGHT and FARNER (this *Bulletin* 1945 v. 42 688) produced evidence to show that the form of *A. punctulatus* Doen known as *moluccensis* Sw and Sw in the New Hebrides should be designated *A. punctulatus farauti* Lav. It was the only form seen there. Whether *moluccensis* and *farauti* are identical or not they were unable to say but expected that this would prove to be the case. LEVER (this *Bulletin* 1945 v. 42 778) also refers to the paper by LAFERAN published in 1902 and considers that the chief vector of malaria in Melanesia hitherto known as *A. (M.) punctulatus* Dön. *moluccensis* Sw and Sw must now be referred to as *A. (M.) punctulatus* Dön. *farauti* Lav.]

The present authors prefer to regard *A. punctulatus*, *A. farauti* and *A. kolensis* as species and not as subspecies of *A. punctulatus* because they can distinguish them in the adult, pupal and larval stages. They also regard *A. farauti* Laveran 1902 as the *A. punctulatus* of Buxton and Hopkins 1927, Paine and Edwards 1929 and Senevet 1931.

In the Solomons *A. punctulatus*, *A. farauti* and *A. kolensis* all occur on Guadalcanal. *A. punctulatus* and *A. farauti* both occur on Bougainville. *A. farauti* occurs in other islands of the Solomons group and also in several islands of the New Hebrides.

*A. punctulatus* is not so common as the other two species and though it feeds readily in captivity does not appear to attack man often in nature in Guadalcanal. *A. farauti* is the commonest species and formed 98 per cent. of the anophelines taken in routine night catches in north west Guadalcanal during a period of over a year. Its normal feeding time is from dusk to dawn, but it will attack man in the daytime in shaded places. It is the principal anopheline attacking man except in the Koli area of Guadalcanal where its place is taken by the strongly anthropophilic *A. kolensis*. H. S. Leeson

LEVI-CASTILLO R. *Anopheles pseudopunctipennis* in the Los Chillos Valley of Ecuador. *J. Econom. Entom.* 1945 June v. 38 No. 3 385-8 3 figs.

ZUKEL, J. W. Marking Anopheles Mosquitoes with Fluorescent Compounds. *Science* 1945 Aug 10 157

Anthracene rhodamine B and fluorescam have been used for marking *Anopheles maculatus* they produce blue, red and green fluorescent colours respectively which can be seen under ultraviolet light. Anthracene can be used either as an aerosol or as a dust mixed with gum arabic. Exposure of the mosquitoes to an aerosol concentration of 10 mgm. per litre of air produces a homogeneous deposit of particles (average size 6.7 microns) on them which is apparently harmless. For use as a dust anthracene 1 part and gum arabic 2 parts are mixed in water the mixture evaporated to dryness and ground to a powder the mosquitoes are dusted with the powder and then placed in an atmosphere of saturated humidity for 15 minutes. The gum arabic prevents contamination of unmarked specimens during the subsequent collection.

Rhodamine B and water-soluble fluorescein are used as dyes made in the same way in the proportion of 10 mgm. of dye to 3 gm. of gum arabic.

Large numbers of mosquitoes (or other insects) can easily be marked and the identification of the marked specimens in the collections examined under ultraviolet light is rapid.

J. F. Corson.

SKUTE P. G. Clinical Observations on Malaria. *Post-Graduate Med J* 1945 Aug v 21 No 238 253-61 10 charts.

An exceptionally clear and succinct account of the clinical features of the different forms of malaria, which deserves to be read by every medical man in Britain, since malaria is likely to be common in returned soldiers. A student of tropical medicine could well base his future reading on this paper which obviously embodies the author's wide and careful personal observations.

Charles Wilcocks.

RAPER A. B. WILSON Margaret E. & WILSON D. B. Dividing Forms of *Plasmodium falciparum* in the Peripheral Blood of Africans. *Trans. Roy Soc Trop Med & Hyg* 1945 Mar v 38 No. 4 291-5

Three cases of malignant tertian malaria are described in African natives in which dividing forms and mature schizonts appeared in the peripheral blood without there being any indication that the infection was running a particularly severe course. In two cases the patients were semi-immune in that they came from districts where malaria transmission takes place for a short period each year. Both these cases might have become seriously ill if treatment had not been carried out. The treatment however was of moderate intensity and this sufficed to bring about a clinical cure. The third case was in a fully immune individual. No treatment was given and the patient never became dangerously ill. The temperature dropped to normal on the fifth day, all parasites disappearing from the blood by the seventh day. In this case the patient had been absent from his home for two years, during which he was exposed to little if any infection. Exposure to a strain of *Plasmodium falciparum* different from the one to which he had been accustomed then took place. The dividing forms and schizonts of *P. falciparum* in these three cases were of the usual type. It is suggested that there may be a race or strain of the parasite in which peripheral schizogony occurs, or that a reticulo-endothelial system overloaded from any cause may allow schizonts to overflow into the general circulation without the grave complications usually associated with their occurrence.

C. M. Wenyon.

PROKOFENKO L. I. [Parasite Carriage and Duration of Malignant Tertian Malaria in Middle Asia.] *Med Parasit & Parasitic Dis.* Moscow 1945 v 14 No 1 45-63 1 fig. [In Russian.]

An account is given of epidemiological and parasitological observations on malaria made by the author between 1942 and 1944 in three collective estates of Uzbekistan (Middle Asia) where severe outbreaks affecting almost 100 per cent. of the population, occurred in 1942.

In February 1943 it was found that, as the result of the epidemic, 10 per cent. of the population were extremely debilitated and anaemic, with protein-deficiency oedema of the face and extremities, while more than 3 per cent. had an enlarged thyroid. The spleen rate was from 19.5 to 24.5 while the parasite rate varied from 40.4 to 59.3. The predominant form of malaria was malignant tertian (383 in 1 094 persons examined or 35 per cent.) with a high proportion

of mixed infections of this and benign tertian while the number of quartan cases was negligible. Between May and October 1942 the entire population of the estates underwent several courses of curative treatment with acrinine [mepacrine] and plasmocide [pamaquin] followed by suppressive treatment.

In addition to this a number of minor hydrotechnical improvements were carried out resulting in a considerable decrease of mosquito-breeding places. In spite of intense treatment which brought about a considerable fall in the spleen and parasite rates the percentage of persons harbouring parasites remained high (5-7 per cent. of the population in summer when the rates were lowest).

The total number of persons kept under observation was 1 143 of whom 801 showed parasites. The majority of these (61.3 to 97.7 per cent.) were symptomless carriers. Paroxysms of fever occurred only in a small minority. The author concludes that carriers represent the main sources of infection leading to epidemic outbreaks in Middle Asia. Their rôle as the reservoir is further enhanced by the fact that 93.1 per cent. of malignant tertian cases harboured gametocytes. Findings of parasites in the same individuals examined from 4 to 9 times were distributed as follows: once in 67.6 per cent. of cases of malignant tertian and in 67.5 per cent. of benign tertian; twice in 24.7 per cent. of cases of malignant tertian and in 25 per cent. of cases of benign tertian. More than 60 per cent. of the repeated findings were made in the new epidemic season and presumably represented reinfections. It was also found that the duration of the infection was longer and reinfections were more common in debilitated underfed persons than in those whose diet was normal. Estimates of the duration of malignant tertian malaria based on the data of mass observations showed that the infection usually lasted 10-12 months. C. A. Hoare

NORONHA A. J. Atypical Malarial Gametocytes in the Peripheral Blood. *Indian Med Gaz* 1945 June v 80 No 6 299. 6 figs. on 1 pl.

LAHA P. N. Malarial Nephritis (with Two Illustrative Case Reports). *Indian Med Gaz* 1945 v 80 No 3 135-7.

The author refers to recently published reports on malarial nephritis and gives detailed clinical notes of two cases. A Hindu boy aged 10 had the characteristic symptoms and signs of nephritis with ascites and oedema. The manner in which the symptoms yielded to small doses of quinine after other treatment had failed to give any alleviation affords presumptive evidence that malaria was the cause of the nephritis. In the second case the rôle of malaria as the primary cause of nephritis was not so convincingly demonstrated. A definite temporary improvement in the patient's general condition followed the administration of quinine but the urine showed no sign of this improvement and uraemic coma was responsible for death a month later. Norman White

YAN TIM WONG. The Measurement of Blood Oxygen in Malaria with the Use of the Oximeter. *Science* 1945 Sept. 14 278-9. 1 fig.

This preliminary note deals with the determination of blood oxygen levels at the time of the paroxysm in ten white subjects undergoing malarial therapy with *P. vivax*. Millikan's oximeter (see below) was used for the purpose of giving a continuous record of the percentage oxygen saturation of haemoglobin in the blood. Coloured patients were found to be unsuitable because of the fact that their skin pigment decreased the amount of light reaching the photo-electric cells and rendered the method less sensitive. Each patient acted as his own control as similar records of oxygen saturation of the blood were made

before inoculation with malaria. The results for each patient were approximately the same before and after inoculation, but varied widely in different patients according to whether they were of an active or lethargic type. During the cold stage of the paroxysm when the patient was cyanosed, the oxygen saturation increased slightly as a result of hyperpnoea. The percentage oxygen saturation then gradually fell as the temperature rose and the extent of the fall was proportional to the severity of the paroxysm—the lowest record showed a 70 per cent. saturation. The reduction in degree of saturation was not compensated by breathing pure oxygen even when accompanied by the intravenous injection of 300–600 cc. red blood cells. During a mild paroxysm the changes in saturation recorded were very small. As the temperature fell, the degree of saturation increased and reached a normal value before the temperature. In some patients the instrument was painfully irritating, especially during the paroxysm, and small doses of codeine had to be administered.

The paper by MILLIKAN (*Rev. Sci. Instruments* 1942, v 13 434) describing the oximeter contains the following paragraph — The oxygen saturation of arterial blood in man can be measured continuously *in situ* by means of bichromatic photo-electric colorimetry of the intact fully flushed ear. The accuracy of the device as determined by gas analysis of arterial blood samples is from 3 to 8 per cent. The term "accuracy" would appear to be more correctly rendered as "error". The entire optical and photo-electric system, comprising a miniature lamp bulb, two color filters and two selenium barrier layer photo-cells, weighs 30 grammes and slips over the shell of the ear. One of the color filters transmits a wave-length band which is equally absorbed by oxy- and reduced hemoglobin thus providing a means of measuring the amount of total hemoglobin in the optical path, independent of its degree of oxygen saturation. The other color is very differently absorbed by the two hemoglobin forms. Several direct reading forms of the instrument are discussed.

J. D. Fulton

NAPIER, L. E. The Present Status of Antimalarial Drugs. *New England J. of Med.* 1945 July 12, v 233 No 2, 38–43. [15 refs.]

In an interesting paper the author describes recent additions to our knowledge regarding the use and relative value of anti-malarial drugs. The conclusions reached are stated as follows —

"Prior to 1942, atabrine was looked on as a valuable addition to the armamentarium of the physician for the cure and suppression of malaria, but its place was certainly second to that of quinine. Recent work has shown that it is probably the most valuable drug in the fight against malaria.

"Despite the fact that quinine and the other cinchona alkaloids have had to take a place below atabrine on the antimalarial priority list, recent work has in no way questioned their efficacy. On the contrary, it has confirmed previous work regarding the antimalarial activity of all the crystalline alkaloids, and more especially that of a mixed alkaloidal preparation which in some of the poorer malarious countries may, on economic grounds, still prove to be the drug of choice for the mass of the population.

"The strict limitations of plasmochin in the treatment of malaria have long been recognized, and recent experience has merely served as a reminder of these limitations. It is, however, the only drug that acts as a true causal prophylactic or actually prevents relapses in benign tertian malaria, albeit in large and dangerous doses. These unique properties should be recognized and, in special circumstances, full advantage taken of them. Furthermore, it seems possible that by a modification of the formula of plasmochin a less toxic but equally efficacious drug may be synthesized. The discovery of such

a drug will give man a weapon with which he will be able to control malaria not only in the individual but in the community. Although it is improbable that malaria will ever be banished by the use of drugs alone with a drug possessing these properties it may be possible to control it in some communities where this was hitherto impossible and in others to do so more effectively and at lower cost than would be possible by any other means. Until however such a drug is discovered no claim for man's mastery over malaria can be made.

*Norman White*

OLDHAM Frances K & KELSEY I E Studies on Antimalarial Drugs The Distribution of Atabrine in the Tissues of the Fowl and the Rabbit. *J Pharm & Exper Therap* 1945 Apr v 83 No 4 288-93 [10 refs]

A study was made of the concentration of mepacrine (atabrine) in the tissues of the fowl and rabbit at various periods after single or repeated intravenous doses. The two species of vertebrate behaved somewhat differently especially in that mepacrine was more rapidly eliminated from the fowl than from the rabbit. When a dose of 5 mgm mepacrine per kgm was given to rabbits intravenously the concentrations at 1 hour later were—Lung 72 mgm. per kgm kidney 66 spleen 46 adrenal 32 liver 20 brain 15 and muscle 3 mgm per kgm. When the sizes of the organs are taken into account it is seen that the liver stores the greatest amount of mepacrine. In the chick little mepacrine is stored in the lungs and with the exception of the liver all the organs store less mepacrine than those of the rabbit. Mepacrine is three times as toxic for rabbits as it is for fowls. In three rabbits which were pregnant it was found that mepacrine crosses the placenta and may become stored in the foetus. Thus when the liver of the mother contained 23 mgm. per kgm the concentration in the liver of the foetus was about 3 mgm. per kgm.

*F Hawking*

JAILER, J W Fluorescent Microscopic Study of the Physiological Distribution of Atabrine. *Science* 1945 Sept 7 258-9

SHANNON *et al* (*J Pharm & Exper Therap* 1944 v 81 307) showed by chemical determinations that atabrine [mepacrine] is localized chiefly in the leucocytes liver spleen and kidney. The present author has used the fluorescence microscope to discover what parts of these tissues contain the drug.

The source of light was an H-4 bulb with a Corning No 5984 filter in front of it and a Corning No 3894 filter in the eyepiece of the microscope. glass lenses were used the wave-length of the transmitted fluorescence being 365  $\mu$ .

Frozen sections from fresh or fixed (formalin) tissue were mounted in saline or 0.2 M  $\text{Na}_2\text{HPO}_4$  (atabrine shows greatest fluorescence at pH 9.5 in aqueous solution).

Adult mice were given intraperitoneal injections of a 2 per cent. solution of atabrine hydrochloride 2 mgm. daily up to totals of 4 to 12 mgm. uninjected mice were controls. The tissue of normal mice shows a slight yellowish fluorescence diffused throughout the section and barely visible at high magnifications (440 $\times$ ) while the fluorescence of atabrine is yellowish-green and so much more intense that the yellowish background becomes invisible.

In the liver the fluorescence was diffusely distributed throughout the parenchymal cells there was little in the Kupffer cells and the sinusoids appeared black. In the spleen the fluorescence was chiefly seen in the Malpighian corpuscles with very little in the sinusoids. This suggests that there was little atabrine in the reticulo-endothelial cells. In the kidney most fluorescence was

seen in the convoluted tubules less in the collecting tubules, and little in the glomeruli. Other organs showed less fluorescence.

As no distinction can be made between atabrine and its degradation products by this method it is unknown whether the fluorescence was entirely given by atabrine

J F Corson

MARKSON J L. & DAWSON J. Investigations in the Chemotherapy of Malaria in West Africa. IV. Report on a Case of Acute Mepacrine Poisoning. *Ann Trop Med & Parasit.* 1945 Oct. 10 v 39 No. 2, 117-18.

A European soldier aged 29 who had been taking suppressive doses of mepacrine for 16 months swallowed, in a fit of mental depression about 250 tablets (25 gm.) in one dose. He began to vomit after ten minutes and vomited 10 to 14 times and the vomiting was soon followed by diarrhoea. He then became weak and drowsy. When seen by the medical officer three hours after taking the mepacrine, he was collapsed and could just be roused. His stomach was washed out a yellow fluid being returned, and he was admitted to hospital at 11.45 p.m., about four hours after swallowing the tablets.

*Conditions on admission*—He was collapsed and stuporose temperature 97.8 pulse (barely perceptible) 80 respirations 22 skin cold and clammy no jaundice and the skin, mucosa and conjunctiva not very yellow cardiovascular and respiratory systems normal liver and spleen normal on physical examination. He was drowsy resented being moved, and could not answer questions pupils contracted reacted to light all tendon reflexes active abdominal reflexes present plantar reflexes flexor

He was given 15 minims of 1/1 000 adrenaline intravenously and gradually improved his blood pressure an hour later was 150/100. An intravenous injection of 5 mgm. of riboflavin was given as a possible antidote to mepacrine, and two pints of 30 per cent. glucose saline were given in four hours by intravenous drip. By the following morning he had recovered and he had no further symptoms.

*Laboratory examinations*—Blood and cerebrospinal fluid were taken one hour after adrenaline had been given and before the glucose saline. Laboratory examinations gave the following results haemoglobin 14 gm. per cent erythrocytes 4,200 000 leucocytes 18 000—polymorph. 82 per cent. lymphocytes 14 per cent mononuclears 4 per cent.—packed red cell volume 42 per cent., blood urea 25 mgm. per 100 ml. blood sugar 90 mgm. per 100 ml. plasma bilirubin 0.5 mgm. per 100 ml., plasma mepacrine 900 $\gamma$  per litre. The cerebrospinal fluid contained no mepacrine. The urine contained no albumin bile sugar or acetone.

The plasma mepacrine was 183 $\mu$  per litre on the third day and 90 $\mu$  per litre on the fifth day the total urinary mepacrine excreted in 24 hours was 2.7 mgm. on the third day and 1.2 mgm. on the fifth day.

Obviously much mepacrine was absorbed and the quick recovery of the patient shows the low toxicity of the drug

J F Corson

FEDOTOV P I. On the Antirelapse Treatment of Benign Tertian Malaria. *Med Parasit. & Parasitic Dis* Moscow 1944 v 13 No 6 54-7 [In Russian]

The author reports satisfactory results of anti-relapse treatment of B T malaria consisting of a minimum of three courses each in three cycles of 5-3 and 3 days with intervals of 10 days between the cycles and of about one month between the courses. The daily doses are as follows. First course—0.3 gm. acriflavine [mepacrine] second and third courses—0.2 gm. acriflavine + 0.04 plasmodicide [pamaquin]. In a group of patients treated according to this

scheme only 3.5 per cent relapsed as compared with 25 per cent. and 15.6 per cent. who had one and two courses of treatment respectively. In untreated control groups relapses occurred in from 25.8 to 98.6 per cent.

C. A. Hoare

PODLESKER A. El cloruro de calcio en el tratamiento de las esplenomegalias palúdicas [Calcium Chloride in the Treatment of Malarial Splenomegaly] *An Policlín Enf Infecciosas del C. A. Videla Hospital F. J. Muñiz*. Buenos Aires, 1942-44 No 4 164-210 15 graphs & 3 figs. [28 refs.] English summary (9 lines)

Clinical notes and haematological studies of a series of patients suffering from chronic malaria with enlargement of the spleen demonstrate the value of chloride of calcium in the treatment of the condition. An intravenous injection of 10 cc. of a 10 per cent. solution of calcium chloride is given on each of five successive days. The injections are given slowly. There is an almost immediate response by the contraction of the enlarged spleen and an amelioration of the associated symptoms. Malarial parasites that have harboured in the spleen are discharged into the peripheral blood stream and so rendered vulnerable to antimalarial drugs.

The claims advanced for this method of treatment are similar to those put forward by advocates of Ascoli's method. [See also this *Bulletin* 1943 v 40 13]

Norman H. Hite

BRUETSCH W. L. The Public Health Aspect of Malaria Therapy of Neurosyphilis. *Amer J Syph* 1945 Sept. v 29 No. 5 494-505 [51 refs.]

ARCH. INST. PASTEUR D'ALGÉRIE 1944 Dec v 22, No 4 380-82 Réglementation de la lutte antipaludique dans l'Empire français. [Organization of the Malaria Campaign in the French Empire]

ANANIAN S. A. CHUBKOVA A. I. AZIZIAN A. A. & KOCHARIAN A. A. [Intermittent Irrigation of Rice Fields as a Prophylactic and Agrotechnical Measure for Malaria Control in Armenian SSR.] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 1 36-45 3 figs. [In Russian.]

The authors describe the results of experiments designed to determine the best method of intermittent irrigation of rice fields as a measure for the control of mosquito breeding. The experimental fields situated in the Armenian republic (Caucasus) were divided into a number of plots some of which served as controls and were irrigated continuously while in others periods of flooding lasting 8-12 days alternated with periods of drying lasting 4, 5 or 6 days. It was found that drying the field 4 days is not long enough to destroy the mosquito larvae. The most satisfactory method is to dry the field for 5 days and then flood it for 8 days. This results in 0.3 per cent mosquito production as compared with that in control plots. Prolongation of the period of irrigation is undesirable since it enables the mosquitoes to complete their development. Though the method of intermittent irrigation somewhat lowers the output of rice it results in an economy of 32.8 per cent of water consumption which can be used for irrigating additional plots under rice.

C. A. Hoare

PARKER W. V. & JOHNSON H. A. A Universal Type Concrete Slab for Precast Ditch Linings. *Pub Health Rep* Wash 1945 May 25 v 60 No 21 582-7 14 text figs. & 2 figs. on 2 pls.

The concrete slab that has proved useful in the lining of ditches of various sectional shapes measures 12 by 24 by 2 inches. It is made with a 1 : 2 : 4



mixture of cement sand and  $3/8$  inch graded gravel mixture. All four edges of the slab are of the tongue-and-groove type. On the long sides of the slab the tongue on one edge and the groove on the other are formed on edges which are at an angle of  $67\frac{1}{2}^\circ$  with the slab surface. The end tongues and grooves are formed on edge surfaces that are at a  $90^\circ$  angle with the slab surface. Figures



FIG 11



FIG 12

Details of the joint between concrete slabs lead to make a  $135^\circ$  angle (fig 11) or a  $180^\circ$  angle (fig 12)

Reproduced from *Public Health Reports* [Washington]

depict the various forms of ditch lining that are possible with this universal slab. The form of joint between the slabs delays the penetration of vegetation through the joints. Details of construction and of ditch lining are clearly described and well illustrated.

Norman White

PRICE M. M. & LYMAN F. E. Second Report on the Control of *Anopheles quadrimaculatus* Say in the Water-Chestnut Areas of the Potomac River 1944. *Pub Health Rep* Wash. 1945 Aug 24 v 60 No. 34 983-94 2 figs.

The control of *A. quadrimaculatus* breeding in the Potomac River where water-chestnut provides very favourable conditions for such breeding was successfully effected in 1943 by airplane dusting with Paris green [this *Bulletin* 1944 v 41 1007]. The presence of numerous malaria carriers in the military forces at Fort Belvoir and the Quantico Marine Barracks during 1944 made a continuation of effective control still more important. The amount of air plane dusting in 1944 was greatly reduced by extensive cutting of the water chestnut which was begun in May. Early cutting prevents reseedling for growth the following year. Once cut the freed plants tend to aggregate into floating mats which are favourable to mosquito breeding until the plants are washed up on shore or swept out into the river. Such temporary breeding was controlled by dusting from boats. Airplane dusting in 1944 was necessary only in the neighbourhood of two of the six military establishments Fort Belvoir and the Quantico Marine Barracks. Only 7 610 acres were dusted in 1944 as compared with 32,538 acres in the previous year. The control was effective. For all six military establishments the mean number of large larvae per 100 dips was 0.52 and the average number of adult female *A. quadrimaculatus* per resting station per observation was 0.6, a comparable figure to that of the previous year when much more extensive airplane dusting was done.

Norman White

BRACKETT S & HUGHES Carrie O Chilling as a means of retaining the Viability of the Sporozoites of *Plasmodium gallinaceum* *J Parasitology* 1945 Aug \ 31 No 4 288-9

In experiments in which chicks are infected by inoculation of sporozoites of *Plasmodium gallinaceum* it is important to get as much uniformity as possible in the infections produced. When chicks are exposed to the bites of infective *Aedes aegypti* mosquitoes only 85 per cent. of them become infected and when COVNEY *et al* [this *Bulletin* 1945 \ 42 865] inoculated infected salivary glands subcutaneously into 200 chicks only 97.5 per cent became infected. For many purposes e.g. drug testing there should be no uninfected birds. The injection of pooled sporozoite suspensions has always in the authors experience and in that of others produced infection.

It is also necessary to have uniformity in the character of the infections. When kept at room temperature the viability of the sporozoites decreases during the hour needed to inoculate intravenously 200 to 300 chickens as is shown by the differences in parasitaemia on the eighth day of infection. The authors colleague Dr WALETZ suggested that the ground up mosquito material should be chilled as soon as possible and kept in an ice bath during the inoculations. This resulted in more uniform infections. The sparing effect of low temperature was also shown by the increased virulence of the chilled preparations as measured by the degree of parasitaemia produced. Oöcyst counts showed that this could not be due to more intense infections in the mosquitoes. Even as short an exposure as 15 minutes to room temperature probably causes marked injury to sporozoites. *J F Corson*

MARSHALL P B The Absorption of Sulphonamides in the Chick and the Canary, and its Relationship to Antimalarial Activity *J Pharm & Exper Therap* 1945 May \ 84 No 1 1-11 [12 refs.]

A study was made of sulphanilamide and eleven derivatives to measure their rate of absorption from the gut and their concentrations in whole blood and in red cells of chicks and of canaries. The drugs are absorbed more quickly and excreted from the blood more quickly in canaries than in chicks. The concentration in the red cells is usually higher in the canary than in the chick. The drugs showed pronounced activity against *Plasmodium gallinaceum* in chicks but they were mostly inactive against *P. cathemerium* in canaries. A blood concentration of 10 mgm sulphadiazine per 100 cc was very active against *P. gallinaceum* to suppress infections of *P. cathemerium* blood concentrations of 60-100 mgm per 100 cc were needed. Generally speaking the degree of antimalarial activity of these compounds in chicks can be correlated with the height of the blood concentration curves. *F Hawking*

## BLACKWATER FEVER

JOURNE H. Le rein dans la fièvre bilieuse hémoglobinoïdique. Etude clinique. Conceptions hystophysiologiques et indications thérapeutiques. [The Kidney in Blackwater Fever] *Méd Trop* Marseilles 1944 May-June-July-Aug \ 4 No 3 225-35

This is a review of the renal signs and symptoms pathology and treatment of blackwater fever. The author considers that the theory of blockage of the renal tubules does not explain the diversity of clinical and biological symptoms which accompany anuria and its development. He asks for instance

how the abrupt onset of anuria can be explained by obstruction of the tubules, unless there develops a sudden simultaneous complete obstruction. He considers the reversibility of the condition an argument against a purely mechanical explanation of the anuria. He points out that the urine often clears of haemoglobin before the onset of anuria suggesting that most of the haemoglobin is already excreted, and that the urine passed in the early stages of recovery from anuria does not contain the cellular and blood debris which might be expected to appear as the result of sudden clearance of obstruction in all the uriniferous tubules. He rightly emphasizes the loss of concentrating power in the post-anuric phase, and suggests that in recovery there is a sudden restoration of (glomerular) filtration in the kidney followed by a slower recovery of the damaged tubules. There is a brief second hand account of the histological appearances of the kidneys, in which the similarity between the lesions of blackwater fever crush injury and incompatible transfusion is noted.

No biochemical investigations of cases other than estimations of urea N have been carried out by the author but he suggests on the analogy of "transfusion nephritis" that there is probably a reduction in plasma chloride and alkali reserve. On these grounds he recommends alkali administration.

The author's main conclusion in this discursive paper is that the cause of anuria in blackwater fever is not yet decided and that precipitation of haemoglobin products may play a part but is not the whole explanation.

B G Macgrath

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### TRYPANOSOMIASIS.

FIERVES R. N. T. W. A Sexual Reproduction Cycle of *Trypanosoma congolense* Broden. [Correspondence.] *Nature* 1945 Sept. 29 390-91

The author describes what he saw through the microscope in fresh preparations of a mixture of a drop of mouse blood heavily infected with *Trypanosoma congolense* and a drop of 0.3 per cent. solution of sodium chloride—he states that the addition of the salt solution to the blood caused sexually mature trypanosomes quickly to become micro- and macro-gametes and conjugate within ten minutes.

The macrogametes were 13-18 $\mu$  long, with somewhat anteriorly placed nucleus, both nucleus and cytoplasm being intensely granular except a posterior area which was clear translucent and swollen. The microgamete 6-8 $\mu$  long with posteriorly placed nucleus and the rest of the body an attenuated filament entered, posterior end first, the translucent area of the macrogamete and was absorbed. A motile zygote is formed, of trypanosome form but tapering from the posterior end. Nuclear material is next concentrated centrally or posteriorly and by contraction of other parts of the body an amorphous oocyst is formed. The oocyst nucleus may after sixty minutes have divided once. The zygote is about 20 $\mu$  in length, and oocyst about half this size.

Oocysts were also seen in skin and lung tissue. "The oocyst appears to form sporoblasts, probably eight, which divide into innumerable sporozoites. The sporozoites break away from the oocyst body and swim actively away by a kind of rolling movement."

The author intends to publish a preliminary paper in which more details will be given, and a full report later. [The question of the occurrence of

syngamy among trypanosomes is discussed in Wenyon's Protozoology 1926 pp 339-340 at that date no reliable evidence of its occurrence had been offered.] *J F Corson*

See also below FULTON J D & GOODWIN T W Studies on the Estimation and Precipitation of Stilbamidine.

See also below FULTON J D & GOODWIN T W The Effect of Light on various Aromatic Diamidines in the Solid State.

## LEISHMANIASIS

HORGAN E. S & SATTI M. H. Penicillin in Kala Azar [Correspondence.] *Nature* 1945 Sept. 8 297

Two adult patients in the Sudan with typical kala azar were treated with penicillin 20 000 units in 4 cc. normal saline intramuscularly at intervals of 3 hours to a total of 1,500 000 units. The result was complete failure—no beneficial effect could be seen and the condition of one patient deteriorated. Gland and spleen smears remained positive.

The authors admit that kala azar in the Sudan is more resistant to treatment than kala azar in India but their experience gave no indication that better results could be achieved by larger doses and continuous administration *Charles Wilcocks*

FULTON J D & GOODWIN T W Studies on the Estimation and Precipitation of Stilbamidine *J Pharm & Exper Therap* 1945 May v 84 No 1 34-41 1 fig [11 refs]

A spectrographic method is described for estimating stilbamidine in biological fluids for the technical details of this the original paper must be consulted. About 2 cc. of serum is required, which was obtained by pooling the blood of several mice. The method measures down to 5  $\mu\text{gm.}$  per cc. with an accuracy of  $\pm 3$  per cent. at levels less than 2  $\mu\text{gm.}$  per cc. measurements cannot be made. When the maximum tolerated dose of stilbamidine is given to mice orally intravenously intraperitoneally or subcutaneously the serum concentration reaches 40  $\mu\text{gm.}$  per cc. within half an hour and then rapidly diminishes. Within 1-2 hours, only traces remain in the blood. Clearly the compound is rapidly absorbed and stored or excreted. When the minimum amounts required to cure infections of *Trypanosoma rhodesiense* are given to the mice the serum contains only traces of the drug. Contrary to what had previously been reported the authors found that absorption of stilbamidine by red blood corpuscles was non-existent or negligibly small. Stilbamidine is precipitated from the blood by many agents including some e.g. trichloroacetic acid metaphosphoric acid, which are used to remove proteins. It is also precipitated by sodium citrate *F Hasking*

FULTON J D & GOODWIN T W The Effect of Light on various Aromatic Diamidines in the Solid State *J Pharm & Exper Therap* 1945 May v 84 No 1 42-5

When stilbamidine 4,4'-diamidino tolane and 4,4'-diamidino- $\alpha$ -methyl stilbene are exposed to sunlight in the dry solid state they often become yellow. The authors found that in spite of this change there was no significant alteration in the absorption spectra, toxicity for mice or therapeutic action (tested

against *Trypanosoma rhodesiense*). Accordingly it is considered that solid specimens of stilbamidine etc. which have gone yellow after exposure to light in the tropics, can still safely be used for human treatment. When one of these yellow samples of stilbamidine is dissolved and then exposed to light it undergoes the same increase in toxicity as unexposed solids do under the same conditions.

F. HANKING

BERBERIAN D. A. Cutaneous Leishmaniasis (Oriental Sore) VI. Treatment with Quinaquine Hydrochloride. *Arch. Dermat. & Syph.* 1945 July, 52 No 1 26-7

In 1838 it was reported by FLAHER (this *Bulletin* 1939 v 36 454) that he had obtained good results in the treatment of oriental sore by infiltrating the surrounding skin with solutions of quinaquine hydrochloride (atebrin). This method of treatment in the hands of other observers gave varying results, though generally it was admitted that early lesions responded well. The author of the present paper tested the treatment in six cases of oriental sore which he had produced on the legs of volunteers by the intracutaneous inoculation in each case of 0.2 cc. of a suspension of culture of *Leishmania tropica* containing approximately 200,000 organisms. All sores were 157 days old when treatment was commenced by injecting 1 to 2 cc. of 10 per cent. solution at weekly intervals. In no case did the treatment favourably affect the course of the disease. It was found on the other hand, that intravenous injections of neostibosan hastened the healing of sores in the ulcerating stage. It was also observed that the subcutaneous injection at bi-weekly intervals of 0.1 to 0.5 cc. of a vaccine of killed culture forms of *Leishmania tropica* (3 to 5 million organisms per cc.) caused sores to ulcerate and thus favoured a rapid healing. [See also this *Bulletin* 1944 v 41 470]

C. M. HENSON

## FEVERS OF THE TYPHUS GROUP

UNITED STATES PUB. HEALTH SERVICE. NATIONAL INST. OF HEALTH. BULLETIN No 183. Studies of Typhus Fever [TOPPING & H. BENGTSON, L. A. HENDERSON, R. G. SHEPARD, C. C. SHEAR, M. J.] pp vi+110 17 graphs. 1945 Washington, D.C. Federal Security Agency U.S. Pub. Health Service

This little volume contains nine Reports dealing with part of the work carried out during the three years, 1943-44 at the Rickettsia Unit of the Division of Infectious Diseases of the National Institute of Health, U.S.A. Hitherto these papers have been distributed to only a small list of workers; the dates on which they would have been published in normal circumstances are shown in the following abstract—no changes have since been made in the texts. Some of the observations have already been incorporated in the present methods of vaccine production.

The volume, appropriately, is dedicated to the memory of one of the authors, Richard Gray HENDERSON who died on October 20 1944 of tsutsugamushi disease (scrub typhus) contracted while he was investigating this infection.

### *Studies of Typhus Fever Vaccines*

(TOPPING, BENGTSON and SHEAR March 27 1942.)

(i) Topping and Bengtson found that the Cox type of vaccine then in use did not cause a great increase in the complement fixation titres of guinea-pigs and that the immunity produced in the animals could be almost completely

broken down by challenge with virulent suspensions of rickettsiae. Other vaccines tested were Craigie's modification of the Cox vaccine Castañeda's rat lung endemic typhus vaccine and Giroud's mouse-lung epidemic typhus vaccine. The percentage of guineapigs in which standard doses of each vaccine caused a rise in the complement fixation titre to 1-64 were —With the Giroud vaccine 63 the Castañeda vaccine 30 the Craigie vaccine 26 and the Cox vaccine 9.5. In the tests of vaccinated guineapigs challenged by very large and equal doses of rickettsiae the average number of days of fever resulting from the challenge were —With the Giroud and Craigie vaccine 0.4 each the Castañeda vaccine 3.6 and the Cox vaccine 4.5. In unprotected guineapigs the average was 9.0 days.

(ii) Topping and Bengtson carried out similar tests with the Cox type vaccine precipitated by alum. When this was given in a single dose of a four times concentration the complement fixation titres were high and the challenged guineapigs had either no fever or only one day of fever. In human tests this vaccine given in two doses produced a higher complement fixation titre than the ordinary Cox vaccine.

(iii) Topping and Shear studied the antigens found in infected yolk sacs that had been treated with ether according to Craigie's method. The supernatant fluid of centrifuged yolk sac suspensions contained important antigens capable of causing positive complement fixation reactions in guineapigs strongly positive Weil-Felix responses in rabbits and immunity in guinea pigs. It was therefore thought desirable to include this soluble antigen in the preparation of vaccines [see also a paper by the same authors in this *Bulletin* 1945 v 42 457].

(iv) Bengtson found that under certain conditions the infecting agent in yolk-sac cultures passed through a Berkefeld N filter. Chick embryos inoculated with the filtrate survived 10-12 days and their yolk sacs usually contained larger numbers of rickettsiae than those inoculated with unfiltered suspensions. Other methods of increasing the yield of yolk sacs are discussed. There was a general degree of correlation between the number of rickettsiae in yolk sacs and the titre of the complement fixation reaction in immunized animals though great individual differences were observed.

A vaccine was prepared by ether treatment of homogenized yolk-sac suspensions without previous centrifugation so that the soluble antigen was retained. After removal of the ether at 37°C and slow centrifugation (1 000 r.p.m. for 10 minutes) the suspension was precipitated by alum.

#### *Epidemic Typhus Demonstration of a Substance Lethal for Mice in the Yolk Sacs of Eggs Infected with R. prowazeki*

(BENGTSON TOPPING and HENDERSON July 31 1942.)

A toxic substance present in rich yolk-sac cultures of *R. prowazeki* killed mice within one to six hours when injected intravenously in sufficient doses which for different cultures were 100 per cent. apart diminishing from 0.5 cc. of a 5 per cent. suspension of yolk sac.

This toxin was destroyed by (1) Heating for half an hour at 60°C (2) formalin at a concentration of 0.375 per cent. (3) treatment with ether for 30 minutes. The substance appeared to be closely associated with the rickettsial bodies because it was absent from the supernatant fluid after high-speed centrifugation and from the filtrate after passage through a Berkefeld N filter. The toxin was neutralized by immune serum.

The number of minimum lethal doses in 1.0 gm. yolk sac was 40-320 in yolk sacs containing very numerous rickettsiae and less than 40 in those containing few rickettsiae.

*Notes on the Preparation of Epidemic Typhus Vaccine*

(TOPPING August 10 1942)

Details are given of a method of preparing the vaccine which was adopted after further study. Its outline the process was as follows:—A 30 per cent. suspension of yolk sacs was homogenized in saline containing 0.75 per cent. phenol and 0.3 per cent. formalin. This was kept 24 hours in a cold room and then made into a 10 per cent. suspension by the addition of saline. To it one and-a-half volumes of ether were added, and it was shaken moderately for one or two minutes in a V-shaped funnel. After keeping for 24 hours in a cold room the aqueous phase was drawn off and freed from ether *in vacuo*. Alum precipitation was still under trial but was not recommended for general use.

*Notes on the Mouse Test with Typhus Vaccine*

(TOPPING August 10 1942)

The power of sera of vaccinated guinea-pigs to neutralize the toxic substance contained in yolk-sac cultures was estimated. Full details are given of the technique.

*Epidemic Typhus Vaccine Preparation of Seed Virus for the Inoculation of Eggs and of Lethal Material for the Neutralization Test in Mice*

(BENGTSON February 19 1943)

The richest vaccines were obtained from yolk sacs infected with dilutions of 1-10 000 of yolk sacs very rich in rickettsiae. The best harvests were obtained from the sacs of chicks still surviving after 6-10 days. More uniform vaccines were obtained by pooling yolk sacs collected over a period of several days and keeping them frozen at a low temperature till used. The longest survival times of inoculated chick embryos and often the richest vaccines were obtained from yolk sacs inoculated with a 10 per cent. saline suspension of yolk sac which had been passed through a Berkefeld V filter. Sometimes, however the filtrate was non-infective. For mouse-neutralization tests very rich yolk-sac suspensions in sterile milk were used.

*Epidemic Typhus Fever Neutralization of the Toxic Substance*

(HENDERSON and TOPPING March 19 1943.)

By an extensive series of experiments it was found that the mouse-neutralizing test served to measure the amount of neutralizing antibody contained in the sera of persons or animals after attacks of typhus fever and after vaccination against the disease. Very high titres were observed in convalescent patients and substantial titres often persisted for several months after attacks. In vaccinated persons the titres were much lower and they declined more rapidly yet they were considerably higher on the average than in vaccinated guinea-pigs.

The test was regarded as an important adjunct to other procedures for the investigation of typhus fever.

*Epidemic Typhus Fever a Study of the Antigenicity of Various Strains of Typhus Virus.*

(TOPPING BENGTSON and HENDERSON September 24 1943.)

Tests were carried out with Breuil, Colombian, and Spanish strains of epidemic typhus rickettsiae and with the Wilmington strain of endemic rickettsiae.

No significant differences were found in the vaccines prepared from the various epidemic strains but guinea pigs vaccinated with the endemic strain had little if any protection against challenge with epidemic strains. Mouse-neutralizing tests gave similar results.

These experiments showed that sharp specific differences existed between the epidemic and endemic strains.

Sera of guinea pigs inoculated with killed typhus antigens showed considerably higher titres of protection against homologous than against heterologous strains of antigen. The differences in the titres after experimental attacks were less pronounced.

#### *Epidemic Typhus Fever Studies of Epidemic Typhus Vaccine*

(TOPPING HENDERSON and BENGTSON February 18 1944)

In April 1942 320 persons were immunized some by two doses of 1.0 cc. of fluid vaccine others by equivalent doses of alum precipitated vaccine. Members of the latter group did not develop complement fixation antibody as consistently or in as high a titre as those vaccinated with equivalent doses of fluid vaccine.

Neutralizing antibodies were developed rather uniformly after vaccination with either type of vaccine and they persisted longer than the complement fixing antigens.

A booster dose of vaccine given some months after the primary vaccination caused a much higher and more persistent rise in both types of antibody than the original vaccination. The neutralizing antibodies were produced more consistently and persisted much longer than the complement fixing antibodies. The agglutination of *Proteus OX10* was not stimulated either by the primary or the booster vaccination.

#### *Technic of a Precipitin Test for the Study of Typhus Fever*

(SHEPARD and TOPPING May 19 1944)

Details are given of the methods of preparing a clear solution of antigen and a potent antiserum. Examples are given to show the applicability of the test to the measurement of antigen and antibody. The use of the test is not limited to intact organisms as is the case with agglutination tests nor to live organisms as in the mouse-neutralizing test. Only two reagents with good keeping properties are needed. For details the original paper must be consulted.

#### *Typhus Fever Antigens of the Rickettsiae of Typhus Fever and the Changes Produced by Heat*

(SHEPARD June 9 1944)

Craigie *et al* are quoted as having shown that when epidemic and murine rickettsiae are heated to 60°C the type specific, heat labile antigens are destroyed whereas the heat stable antigen common to both types is not affected (CRAIGIE *et al* 1943 Memorandum No 7 Project Med 8 National Research Council of Canada).

In the present study Shepard used the precipitin complement fixation and mouse-neutralizing tests. The sera of rabbits immunized by heated epidemic and murine rickettsiae did not give a positive precipitin reaction with unheated antigens but they did react with heated antigens. Sera of rabbits and guinea pigs immunized with heated antigen contained no neutralizing antibodies and the guinea pigs were still susceptible to challenge with virulent rickettsiae. It appeared therefore that the heat-stable antigens



were not concerned in the production of immunity they were also found to have little epidemic or endemic type-specificity and to have a broadened range of reaction with the precipitin test so that for example they gave positive reactions with sera of animals immunized against *Proteus O\19*.

From these and other observations recorded in the paper the author concludes that the cross immunity between epidemic and murine typhus is not due to the absence of specificity in the heat-stable antigens, but to a similarity of the unheated antigens.

John W D Megaw

GREIFF D & PINKERTON H Effect of Enzyme Inhibitors and Activators on the Multiplication of Typhus Rickettsiae. II. Temperature, Potassium Cyanide and Toluidin Blue. *J Exper Med* 1945 Sept 1 v 82 No 3 193-206. 16 refs.

The present study is in continuation of work already done by the authors in which they showed that penicillin and para-aminobenzoic acid (PABA) inhibited the growth of typhus rickettsiae in the yolk sac. [See this *Bulletin* 1945 v 42, 362.

In the present experiments murine rickettsiae of the 45th passage were used. The authors found that the following factors affected the growth and multiplication of rickettsiae in the endodermal cells of the yolk sacs of hens eggs —

(1) Reduction of the time of blending of the infecting suspensions from four minutes to ten seconds caused a considerable average increase in the multiplication of the rickettsiae. (2) Eggs of Wyandotte hens yielded scanty cultures as compared with eggs of White Rock hens in which growth was abundant. It was thus possible to obtain cultures of varying richness for different types of experiment. (3) Growth was much more active in eggs incubated at 37.5°C than in those incubated at 40°C. (4) Suitable doses of potassium cyanide solution introduced into the yolk sacs greatly stimulated the growth of rickettsiae presumably by depressing the metabolic activity of the cells. (5) Toluidin blue delayed the development of rickettsiae by about three days, but the inhibiting action wore off as the dye became decolorized, and repeated injections were impracticable. (6) The inhibiting action of a temperature of 40°C was neutralized by potassium cyanide but the similar action of toluidin blue was not affected, so that the mechanism of inhibition have been different. (7) The inhibiting action of PABA was not neutralized by potassium cyanide.

Several compounds related to PABA were tested but no inhibiting action was detected.

John W D Megaw

GRENOUILLEAU G L'épidémie de typhus en Algérie (1941-1942-1943). [The Epidemic of Typhus Fever in Algeria (1941, 1942, and 1943). *Arch Inst Pasteur d'Algérie* 1944 Dec v 22, No 4 353-79 4 graphs.

The incidence of louse-borne typhus in Algeria during each of the four successive seasons October to the following September was as follows — 1939-40 11,874 1940-41 55,530 1941-42, 193,352 and 1942-43 45,408. The seasonal incidence was of the usual type for example there were 306 cases in October 1941 and a steady rise reaching the peak figure of 6,106 cases in March 1942. High but gradually declining figures were recorded in April, May, and June. In July a rapid fall set in, and in September the figure was 352. The author believes that all the official figures ought to be multiplied by five or six to give a true estimate of the number of cases that actually occurred.

Considerable importance is attached to the carry-over of infection by the dried faeces of infected lice and possibly of fleas though mild and inapparent attacks in children are also important. The fatality rate among the indigenous population was 22 per cent among Europeans it was 30.7 per cent ranging from 5 per cent in children of 10 years and under to 100 per cent in persons over 70.

More than 3½ million doses of Blanc's live murine vaccine were administered between December 1941 and January 1944. The Durand and Giroud killed vaccine was administered to 297 000 persons. Examples are given of the striking success that resulted in several localities from the use of the Blanc vaccine which however had the drawbacks of causing attacks of murine typhus in 5-6 *per mille* of the persons vaccinated and of being somewhat unreliable at times. There never was the slightest reason to suspect that murine infection was introduced into any locality as a result of the use of the vaccine. The killed vaccine of Durand and Giroud had been given to 13 medical men who subsequently contracted the disease but none of them died. There were 14 deaths among 19 non vaccinated medical men so that the life saving effect of the vaccine was clearly demonstrated. It is also stated that no death was known to have occurred among the 297 000 persons protected by this vaccine which was also completely safe. The chief drawbacks of the killed vaccine were the necessity for giving two or three doses and the short duration of the resulting immunity which was estimated to be six months against about three years in the case of the live vaccine.

LAURET is said to have already developed a murine live vaccine prepared from the brain of the white mouse and applied by scarification of the skin.

The Pasteur Institute of Algeria is producing a killed vaccine for use in a single dose of 2 cc and specially intended for communities which are already partly immune to the disease.

In a footnote it is claimed that the measures adopted have brought the epidemic under control in conditions in which it would have been expected to persist during the first six months of 1944 only 874 cases were reported. The chief credit is given to vaccines, disinfection and disinfection on the necessary scale were found to be impracticable in the conditions that existed during the epidemic. A supply of DDT obtained from the Rockefeller Foundation was strikingly successful in the localities in which it could be employed.

John H. D. Megaw

MACCHIAVELLO A. & CIFUENTES O. Significación epidemiológica de los caracteres clínicos del tipo exantemático al final de una epidemia. [The Epidemiological Significance of the Clinical Features of Exanthematic Typhus Fever at the End of an Epidemic.] *Rev. Chilena de Hig. y Med. Preventiva* 1945 Mar v 7 No 1 15-33. English summary.

The authors present a critical statistical analysis of the chief clinical features of 225 cases of louse borne typhus observed between May 28th and September 2nd 1939. During this period the 1937-39 epidemic in Santiago was coming to an end and the authors conclude that at such a time the number of mild and atypical attacks tends to increase, so that cases are likely to be missed unless this matter is borne in mind.

Although the fatality rate of 24 per cent does not suggest that the disease was of a specially mild type a number of interesting points are brought out in the tables and in the text.

After a primary defervescence and clinical cure 69 of the patients had a recurrence of the fever lasting one to three days but without special symptoms and the temperature seldom rose as high as 39°C. In some severe cases the

temperature fell to normal before the signs and symptoms had completed their evolution. The termination was by crisis in 51 cases and by lysis in 75. In the others the secondary rise of temperature occurred or the termination could not be observed.

Among 182 cases the duration of the fever was 3-6 days in 3, 7-8 days in 9, 9-12 days in 73, 13-16 days in 60, and 17-24 days in 17.

The Weil-Felix titre rose to 1-160 or over in 214 of the 225 cases. Relatively low titres of 1-160 and 1-320 occurred in 75 patients of whom 14 died. In the remaining 139 patients the titres were 1-600 or 1-1 000 and among these there were only eight deaths.

Complications involving the lungs occurred in 74 cases. pneumonia occurred in 12 cases, severe bronchitis in 7, bronchopneumonia in 4, pleurisy and acute laryngitis in 2 each. There was only one case of suppurative otitis, parotitis, thrombosis or haemorrhage are not mentioned in the text or shown in the table.

John W D McGee

FALIN, L. L. [Changes in the Nervous Elements of the Skin and some other Organs in Typhus Fever.] *Byull. Eksper Biol i Med* Moscow 1945 v 19 No 3 33-7 3 figs. [In Russian.]

With a view to throwing light on the mechanism of the vasomotor secretory and trophic disturbances in typhus fever the author has studied the changes undergone by the terminal portions of the peripheral nervous system. Special attention was devoted to the histopathology of the nerve fibres and endings in the skin, since—like the central nervous system—this is one of the chief regions where the characteristic vascular changes occur. For comparison, a study was also made of the corresponding nervous elements in the epiglottis.

As the result of this investigation the author arrives at the following conclusions: (1) In typhus fever the elements of the peripheral nervous system of the skin and epiglottis are markedly but irregularly affected. (2) The changes undergone by the nerve fibres are usually degenerative but in some cases they are due to irritation. (3) The sensory nerve endings in the skin of the type of Meissner's and genital corpuscles (the end-bulbs of Krause in the glans penis) usually retain their normal structure but some exhibit phenomena of irritation in the form of globular thickenings (*Angel'sk nomen*) at the end of the terminal filaments. (4) In view of the relatively good preservation

the sensory nerve endings and of the thick myelinated fibres in the skin in the epiglottis it would appear that the majority of degenerated nerve fibres observed in the nerve plexuses belong to the vegetative and in particular to the sympathetic system proper.

C A Hoare

YEOMANS, A. SKYDER, J. C. & GILLIAM, A. G. The Effects of Concentrated Hyperimmune Rabbit Serum in Louse Borne Typhus. *J Amer Med Ass.* 1945 Sept. 1 v 129 No 1 19-24 [Refs. in footnotes.]

Concentrated hyperimmune rabbit serum, prepared by the Lederle Laboratories was administered to 25 patients who had not been vaccinated against typhus at the Cairo Fever Hospital in a ward placed at the disposal of the U.S.A. Typhus Commission. The patients were Egyptians aged 18-48 years in whom the time of onset of the fever was clearly less than seven days. For reasons "not pertinent to this discussion" the system of alternate controls was not adopted, but 44 other cases comparable in all respects except as to the dates of onset served as controls.

Each patient was tested for sensitiveness to rabbit serum by intradermal injection of 0.1 cc. of a normal animal's serum. the response was observed

after 20 minutes. The specific serum was injected daily intravenously intramuscularly or usually by both routes. The initial dose was 1.0 cc. for each pound of body weight; the later doses were 0.25 cc. for each pound of weight. Intravenous injections were given at a rate of not more than 0.5 cc per minute for the first 5 cc. and afterwards a rate of 4 cc. was never exceeded. Chills occurred in seven cases probably because of imperfectly prepared glassware. Vomiting occurred in one with a fall of 24 mm. in the systolic blood pressure. Nausea occurred in two with a fall of 16 mm. in the systolic pressure. Headache was caused or increased in 11 cases. Intramuscular injections of serum up to a maximum of 115 cc. in 24 hours were made into the buttocks. The average quantity of serum given to each patient was 188 cc. the range was 51 to 512 cc. The duration of the treatment varied from one to six days.

No death occurred among the 25 treated patients; there were eight deaths among the 44 controls. The average duration of the fever in the treated subjects was 13 days; in the controls it was 18½ days. The most convincing evidence of the efficacy of the treatment was the remarkable mildness of the attacks in the 10 patients whose treatment was started on the second or third day; in seven of these the attacks were exceptionally mild; in two it was moderately severe and in one it was severe. The fever lasted for only seven or eight days in four of these patients; it lasted for 10-14 days in five and for 17 days in one. A comprehensive analysis of the chief features of the cases is presented in tabular form. Seven of the patients had serum sickness. Rickettsiae of the epidemic type were isolated from 18 of the 25 patients.

It was concluded that the serum had a favourable therapeutic effect when the treatment was started within the first three days of the illness, when started later its value could not be determined with certainty. From the data available it appeared that para-aminobenzoic acid had a more definitely favourable effect on patients who came under treatment after the third day [see this *Bulletin* 1945 v. 42, 201].

The serum is available in very limited quantities and presumably it is very costly, so that its use is likely to be restricted to medical or sanitary personnel over the age of 40 and it would be specially needed by patients who had not been vaccinated or who had been incompletely vaccinated.

*John W. D. Megaw*

ALLEN A. C. & SPITZ Sophie. A Comparative Study of the Pathology of Scrub Typhus (Tsumugamushi Disease) and other Rickettsial Diseases. *Amer. J. Path.* 1945 July v. 21 No. 4 603-81 88 figs. (14 coloured) on 18 pls. [57 refs.]

This study was carried out at the Army Institute of Pathology, Washington. The tissues investigated came from 74 cases of scrub typhus in the New Guinea area, from 24 cases of epidemic typhus in Egypt and from 12 cases of Rocky Mountain spotted fever. The paper is illustrated by 86 excellent photomicrographs of which 14 are coloured. It deals almost entirely with the morbid histology of the diseases and one special object of the study was to determine whether any of the changes observed in mite-borne typhus were sufficiently characteristic and constant as to permit a histological differentiation of the various typhus fevers.

The study is of special value because of the wealth of material that was available and because this material was thoroughly investigated by a single team of highly skilled observers. [The findings however cannot be regarded as universally applicable in all respects to each of the three typhus fevers. All of these are known to show a wide range of variability in their clinical aspects so that although the morbid histology of each may conform to a single

general pattern considerable variations in the details of the pattern can be expected to occur in different outbreaks of the disease. The descriptions of the morbid histology of louse-borne and mite-borne typhus by various competent observers provide clear evidence that these variations do occur. This comment does not detract from the great intrinsic value of the paper.]

In the detailed description of the eschar of scrub typhus the important part played by secondary, chiefly staphylococcal infection is clearly shown. The lesion begins as a vesicle which soon becomes a pustule associated with a strictly local thrombophlebitis and arteritis of a septic type—the rickettsial reaction is seen in the veins at some distance from the central area. It takes the form of a mononuclear infiltration of the vessel walls—sometimes there is also swelling of the endothelial cells and occasionally non-occlusive thrombus is seen.

In the skin macules the equivalent of the "typhus nodule" is seen in the arterioles, capillaries and veins—the changes observed in these vessels "appeared to constitute an expression of intrinsic vascular usually intimal damage."

The macules of louse-borne typhus are essentially similar but the capillary thrombi, though less constantly present, are more conspicuous when they do occur and the endothelial cells are more obviously damaged—there is also a tendency to a necrotizing arteritis which is not found in scrub typhus. The macules of Rocky Mountain spotted fever and also of boutonneuse fever resemble those of louse-borne rather than of mite-borne typhus.

The vascular changes found in other parts of the body are of the same general type and the conclusion is reached that arteritis is exceedingly slight in scrub typhus in contrast with epidemic typhus and Rocky Mountain spotted fever."

The percentage incidence of some of the chief findings is shown in the following table which has been compiled from the tables and other information contained in the paper—

	Scrub Typhus	Epidemic Typhus	Rocky Mountain Fever	Remarks
Interstitial myocarditis	93	83	83	In all three groups there was a remarkable degree of preservation of the myocardial fibres.
High-grade interstitial myocarditis	49	33	25	
Interstitial pneumonitis	55	35	9	
Bacterial bronchopneumonia	30	8	20	Most pronounced in scrub typhus.
Hyperplasia of lymph nodes	100	Usual	Usual	
Necrotic areas in lymph nodes	33	0	0	
Diffuse glomerulonephritis	30	78	50	
Typhus nodules in pons cerebri	33	81	?	
Typhus nodules in grey cortex	10	83	Nil	

The nodules of scrub typhus are similar in type to those of epidemic typhus the corresponding lesions in Rocky Mountain fever are microinfarcts distributed in the white matter of the cortex which was never invaded by the nodules of the other two diseases

The histological changes observed in the liver spleen pancreas adrenals and gastrointestinal tract were essentially similar in all the three groups of typhus fevers. The authors do not accept the view that the vascular atony and increased permeability observed in epidemic typhus are due to structural damage to the vessels caused directly by the presence of the rickettsiae it is pointed out that vasomotor collapse is just as striking a feature of scrub typhus as it is of epidemic typhus so that the histological findings do not support the mechanistic view. A humoral mechanism is regarded as a more likely explanation and evidence was found of damage to the cortical cells of the adrenals so that the question of adrenal insufficiency deserves consideration. Reasons are given for regarding the effects of the rickettsiae as being largely due to allergic action and reference is made to the basic clinical aetiological and in many respects immunological similarities between scrub typhus and the other rickettsial diseases. The authors classify the human rickettsioses in four groups —

I The Typhus Group (louse-borne and flea borne) with *Proteus* O\19 Weil Felix reaction

II Spotted Fever Group (tick borne) with indeterminate Weil Felix reaction

III Tsutsugamushi fever group (larval mite borne) with O\1A response

IV Miscellaneous Group all with negative Weil Felix reactions. In this group are included Q fever believed to be tick borne trench fever which is louse-borne and the two problem fevers of North America Colorado and Texas tick fevers of which it is stated that proof of the rickettsial aetiology of these diseases is not yet universally accepted. John W' D Megaw

SETTLE E B PINKERTON H & CORBETT A J A Pathologic Study of Tsutsugamushi Disease (Scrub Typhus) with Notes on Clinicopathologic Correlation. *J Lab & Clin Med* 1945 Aug \ 30 No 8 639-61 15 figs. [23 refs.]

The lesions occurring in tsutsugamushi disease in man and experimental animals are described in detail the paper is illustrated by 15 clear reproductions of good photomicrographs

The authors classify the human rickettsial diseases excluding the moot problem of trench fever into (1) typhus human (carried by lice) and murine (carried by fleas) (2) spotted fever (carried by ticks) (3) tsutsugamushi fever (carried by mites) and (4) Q fever (infection found in ticks but epidemiological studies are incomplete). This classification is said to be definitive on immunological grounds [The name spotted fever when divorced from the qualifying words Rocky Mountain is certainly not definitive.]

The present study is based on 55 fatal cases among American troops stationed in and near New Guinea. Special attention has been given to a comparison of the pathology of tsutsugamushi fever with that of typhus and spotted fever it is stated that in all these diseases the pathological changes are direct results of the multiplication of rickettsiae in the endothelial cells or smooth muscle cells of the blood vessels and that the organisms cause swelling and proliferation of the endothelium cellular infiltration of the vessel walls perivascular accumulation of mononuclear cells and occasionally thrombosis and haemorrhage. Epidemic typhus and spotted fever are said to have remarkably similar histopathological features except that the tendency to

The present patient was employed at a water works in Ingham, North Queensland in the course of his work he walked through drains and under growth near the river bank. There was no history of a bite by a tick or other arthropod.

For the first 12 days of the illness there was relatively high fever of a deeply remittent type with heavy daily sweats for the following 19 days there was a daily rise of temperature but to a lower level. The onset was with cough and blood-stained sputum so that a diagnosis of pneumonia was made. During the second week oedema of the ankles and ascites appeared, and the sweats ceased. In the third week signs of heart failure and jaundice occurred. The fever declined gradually and all the symptoms disappeared with the exception of deafness which had set in at an early stage.

The serum-agglutinating titres for *Rickettsia burneti* were 1-30 on the 28th day and 1-1 000 on the 55th day for *Proteus OXX* they were 1-80 on the 28th day and nil on the 55th day.

This was the first case confirmed as occurring in North Queensland it narrows the gap between the endemic centres of Q fever in Queensland and Montana U.S.A. by a mere 500 miles.

Bandicoots and cattle were numerous in the locality and the bandicoot tick *Haemaphysalis humerosa* has been reported by HEASLIP as occurring in North Queensland.

John W D McGaw

## YELLOW FEVER.

BATER, M. & ROCA-GARCIA, M. Laboratory Studies of the Salmiri-Haemagogus Cycle of Jungle Yellow Fever *Amer J Trop Med* 1945 May v 25 No 3 203-16 2 figs. [24 refs.]

The authors have maintained a Colombian strain of yellow fever virus through five cycles in the laboratory using Salmiri monkeys as hosts and the mosquito *Haemagogus capricornis* as the vector. Details are given of the methods employed in keeping the mosquitoes in the laboratory. Wild-caught *Haemagogus* were used in all the experiments for there has been no indication of the presence of yellow fever virus in the study areas since 1940. Similarly wild-caught Salmiri monkeys were used, but only animals whose sera was previously found negative in the yellow fever protection test.

The yellow fever virus used in the transmission experiments had been recently isolated from a patient (Perez) who died of the disease contracted in the Restrepo area north of Villavieja.

This strain produced variable results when inoculated intracerebrally into adult white mice, but 3- and 5-day-old mice were highly susceptible. It was highly virulent for Salmiri monkeys and 8 out of 10 animals infected by mosquito bite died of acute yellow fever.

The extrinsic incubation period in *Haemagogus capricornis* was found to be 22 to 24 days at 24 to 27°C and 13 to 15 days at 30°C. Only a certain percentage of the mosquitoes became infected after feeding on monkeys containing virus in the blood. The percentage infected seems to depend on the amount of virus ingested and the temperature at which the mosquitoes are kept.

The authors discuss the correlation between factors influencing the *Haemagogus* infection in the laboratory and the natural habits of the mosquito. The relatively high temperature necessary for infection is obtained by the species frequenting sunny localities in the forest canopy where the temperatures are higher than in the lower forest strata. Moreover the habits of the Salmiri monkeys in the Villavieja area closely correspond with those of *Haemagogus*.

In view of the fact that Samurís are the commonest local primates and *Haemagogus* the most abundant Aedine mosquito one might have expected a higher incidence of yellow fever infection among them but possibly the high mortality rate may account for the relatively low rate of positive protection tests (10 out of 81) most animals not surviving the infection. *E Hindle*

WADDELL, Mary B & TAYLOR R M Studies on Cycle Passage of Yellow Fever Virus in South American Mammals and Mosquitoes Marmosets (*Callithrix aurita*) and Cebus Monkeys (*Cebus versutus*) in combination with *Aedes aegypti* and *Haemagogus equinus* *Amer J Trop Med* 1945 May v 25 No 3 225-30 3 figs [14 refs.]

An investigation of the cyclic transmission of yellow fever by means of alternate passage through insect vector and vertebrate host with the object of helping to determine the way in which virus is maintained in certain forested regions of South America.

Three virus strains were used two Brazilian, isolated from non fatal cases of jungle yellow fever and one Colombian, isolated from a rhesus monkey infected by the bites of wild *Haemagogus* caught in the forests of Volcanes.

In the first series of experiments a marmoset *Callithrix aurita* was inoculated with virus and when the virus titre of this animal was high, *Aedes aegypti* were fed on it. These mosquitoes were kept at 26° to 28 C. for 28 days and then fed on a normal marmoset. From then on the host vector host cycles continued until the ninth cycle. No marmoset exposed to bites failed to become infected and all showed virus when first tested on the 2nd or 3rd day. 15 out of 17 died on the 4th to the 8th day. The two which recovered showed virus up to the 4th and 5th days respectively and were immune when tested on the 21st day.

A similar series was carried out with Cebus monkeys *Cebus versutus* and *Aedes aegypti* through five complete cycles. All the exposed monkeys showed circulating virus but only one out of 13 died of the infection. Those that recovered developed immunity. The virus was present in the circulation on the 3rd to the 5th days and may persist to the 7th day. The concentration was low compared with that found in the marmoset. Two cycles were also completed with the Colombian strain.

Another series was conducted with marmosets and *Haemagogus equinus*. Only three cycles were completed and four successful transfers obtained. There were also three failures but in two the incubation period in the mosquito was near the minimum and in the third failure only one mosquito was involved. In one experiment three *Haemagogus spegazzinii*, a species found in regions in Brazil where jungle yellow fever is endemic were able to transmit the virus from an infected to a normal marmoset.

The results of these experiments support the view that the virus may be preserved in forested areas by passage through sylvan mosquitoes and monkeys but do not exclude the possibility that other vertebrates and arthropods may play a rôle in the epidemiology of jungle yellow fever. *E Hindle*

LAEMMERT H W Jr & DE CASTRO FERREIRA, L. The Isolation of Yellow Fever Virus from Wild-Caught Marmosets. *Amer J Trop Med* 1945 May v 25 No 3 231-2.

A record of the isolation of yellow fever virus on four occasions from wild marmosets *Callithrix penicillata* caught between June 7th and August 13th in a sharply delimited locality in the neighbourhood of Ilhéus Bahia where jungle yellow fever is endemic. All four animals were in poor physical condition



when caught and died with gross lesions suggesting yellow fever subsequently confirmed by animal experiments and histopathological examination. Later 1437 other marmosets have been obtained without any more cases of yellow fever infection being discovered.

"Yellow fever virus has never been isolated previously from naturally infected vertebrates other than man. *E Hindle*

SMITHBURN K. C. & MAHAFFY A. F. Immunization against Yellow Fever Studies on the Time of Development and the Duration of Induced Immunity *Amer J Trop Med* 1945 May v 25 No. 3 217-23. [13 refs.]

The authors investigated the results of immunization with the attenuated yellow fever virus 17D in both monkeys and human beings.

Twelve rhesus monkeys were vaccinated subcutaneously and after intervals ranging from one to fourteen days they were tested for immunity by the inoculation of a standard dose of yellow fever virus (Asibi strain). Protective antibodies were found to develop within six or seven days, but the monkeys were completely resistant at least 24 hours before the appearance in the serum of protective bodies, i.e. within five or six days after vaccination.

Ten adult male African volunteers, each non-immune to yellow fever were similarly vaccinated, and protective antibody was found to be present in most cases by the 10th day after injection of 17D vaccine, and may be present on the 7th day. The results of post vaccination surveys of immunity in persons inoculated in Africa with 17D vaccine prepared in New York indicate that 92.2 per cent of soldiers sampled 1 to 22 months after vaccination showed protective antibodies. Ninety per cent. of civilians inoculated in Kenya gave positive protection tests 23 to 36 months after being vaccinated. More than 90 per cent of persons vaccinated in Uganda had protective sera after 3 years, and there was no decline in the incidence of immunity in the third year. Finally the percentage of children who became immune as the result of vaccination was as great as that of adults and the antibody response was equally well maintained. *E Hindle*

FOREIGN OFFICE. International Sanitary Convention, 1944 modifying the International Sanitary Convention of June 21 1926. Washington, Jan. 5 to 15 1945 [Cmd. 6637 (Session 1944-45)] (Miscellaneous No 7 1945) 15 pp. London H.M. Stationery Office. [3d]

— International Sanitary Convention for Aerial Navigation, 1944 modifying the International Sanitary Convention for Aerial Navigation of April 12, 1933. Washington, 5th-15th January 1945 [Cmd. 6638 (Session 1944-45)] (Miscellaneous No 8 1945) 16 pp. London H.M. Stationery Office [3d]

Further recommendations have been made on the delineation of yellow fever areas, to include part of N Rhodesia and changes in S America. [See *Bulletin of Hygiene* 1946 v 21 1]

## PLAGUE.

ROTMAN C. M. H. Bubonic Plague in Dakar *J Roy Soc Med. Ser.* 1945 July v 31 No. 3, 155-8.

Much of the interest of this account is due to the occurrence of the epidemic in the French port of Dakar. Infection of the rat population of the dockyard

seems to have come from - up-country via the railway but human bubonic plague is evidently an almost annual occurrence in Dakar itself.

Rodents along the two hundred mile coastal belt up to St. Louis and also in Senegal and in Mauritania are liable to epizootic plague. This is the animal reservoir from which Dakar becomes infected. The present considerable epidemic maintained an essentially native background. A vaccination campaign was started by the French authorities who used the living attenuated Madagascar vaccine. British and American personnel received the usual killed vaccine. Each individual vaccinated obtained a *passport sanitaire* which gave him a freedom of movement not permitted to the unvaccinated. Even those who had received killed vaccine however could not qualify for the passport without submitting to inoculation with living vaccine because the French medical authorities had no faith in the killed vaccine. A considerable reaction developed in many cases from the living vaccine in a dose of 1 cc given in the scapular region with the result that many people had tissue sloughs at the site of inoculation. It appeared that the French population and even the medical authorities took a detached view of the outbreak as they considered that plague in Dakar was a disease of natives only. When the human cases became more frequent and infected rats were no longer found, the possibility of transmission by human contact was considered. This led to the dusting of clothes of native dockyard workers with 10 per cent DDT powder to kill fleas. Treatment of plague cases at the isolation hospital was symptomatic. An interesting documentary film of the outbreak was made and this may be useful for the training of public health workers.

W F Harvey

WHEELER C. M & DOUGLAS J R Sylvatic Plague Studies. V The Determination of Vector Efficiency *J Infect Dis* 1945 July-Aug v 77 No 1 1-12 1 chart [2] refs.]

It is very desirable to have a simple standard measure of vector efficiency as a basis of comparison for different species. This vector efficiency a numerical value determined experimentally is represented by the average number of transmissions effected by a given individual flea of any species. Any normal flea may be considered to have three inherent potentials (1) infection potential (2) vector potential and (3) transmission potential. [See this *Bulletin* 1942 v 39 616 and 1943 v 40 695] The details of experimentation should be consulted. After finding that a flea species was capable of transmission the procedure was to feed the laboratory reared flea infected from an animal with a known bacteraemia, daily on single white mice as long as the flea lived. An example will make the mode of calculating efficiency clear. If 100 fleas of the same species are given an opportunity to become infected and 80 of them acquire the infection, the *infection potential* would be 0.80. If of the 80 infected fleas 40 became infective the *vector potential* would be 0.50. If the 40 infective fleas transmit the infection 80 times the *transmission potential* would be 2. The product of these potentials—0.80 0.50 and 2 represents the vector efficiency of the species tested. Four species of fleas were tested individually and gave the following vector efficiencies *Ctenocephalides felis* 0; *Hoplopsyllus anomalus* 0 *Xenopsylla cheopis* 0.43 and *Diamanus (Ceratomyx) montanus* 0.84.

W F Harvey

RUMREICH A. S & WYNN R. S. A Study of the Rodent-Ectoparasite Population of Jacksonville, Fla. *Pub Health Rep* Wash. 1945 Aug 3 v 60 No 31 885-905 2 figs [40 refs.]

SAVINO E. Aplicación al hombre de la vacuna antipestosa cepa E. V de Girard. [Living Plague Vaccine for Man.] *Bolet Sanitario*. Buenos Aires. 1943 Apr.-June v 7 Nos. 4 5 & 6, 103-11

It is evident that the use in vaccination of living non-virulent, but immunizing plague strains is making headway. The strain employed in the province of Córdoba, Argentina, was the E.V. strain of GIRARD. Thirty persons were vaccinated and careful notes made of reaction with the following conclusion. None of the persons suffered any grave disability, all were able to continue at their daily work in spite of some pain, a little rise of temperature and local reaction. With the subsidence of this reaction there remained a small subcutaneous nodule. The author approves of the vaccine on the ground of its efficacy, experimentally in the guinea-pig and of some years application in man. It should find a use especially in those districts where climatic conditions are favourable to development of plague outbreaks. *W F Harvey*

### BACILLARY DYSENTERY

LAWRENCE E. A. & BENNETT R. E. A Study of Diarrhoea occurring at Army Air Force Headquarters, Calcutta, India. *J Amer Med Ass* 1945 Sept. 15 v 129 No. 3 194-6.

An American air base was situated on the Hooghly River in the midst of a densely populated (about 14 000 persons within half a square mile) collection of Indian villages where extremely insanitary conditions prevailed. The village streets and fields are littered with all kinds of debris. Decaying garbage, human and animal excreta and occasional foul-smelling carcasses of dogs and bullocks left lying for days at a time are the usual conditions found.

From January to June 1944 509 soldiers reported sick with diarrhoea and in July there were 205 cases the sudden increase being due to the onset of the rainy season and increase in fly-breeding. A careful study of 198 consecutive cases of diarrhoea was made from July 11th to August 2nd; they included 31 cases of amoebic dysentery, 66 of bacillary dysentery and 7 of both amoebic and bacillary dysentery. Fever was present in 16 of the amoebic dysentery cases and in 31 of the bacillary dysentery cases, hence it has little diagnostic value. Tenesmus was present in 5 of the amoebic dysentery cases and in 19 of the cases of bacillary dysentery. *Shigella* organisms were isolated from 25 of the 66 cases of bacillary dysentery, no *Shiga* type was isolated.

Control measures included spraying of fly breeding places with DDT or pyrethrum, fly-trapping and screening of buildings and the resulting fly control was dramatic and gratifying. Indians working in and near mess halls were given a daily dose of carbarsone grain  $\frac{1}{4}$  for 10 days, and repeated stool examinations were made on food-handlers. From August 2nd to 23rd there were 21 cases of bacillary and 11 of amoebic dysentery, a slight decrease only though there was a greater decrease in the total number of diarrhoea cases. American soldiers were also a reservoir of infection and, as many lived at the hotels for various periods, control could not be very complete.

The chief conclusions are that careful diagnosis is necessary so that thorough treatment may be given, and that sanitary discipline should be strictly maintained. *J F Corson*

BOSE A. N. & GHOSH, J. K. Sulphanilyl Benzanilide in the Treatment of Bacillary Dysentery. *Indian Med Gaz.* 1945 June v 80 No. 6 293-4

Twenty-one cases of bacillary dysentery were treated with sulphanilyl benzanilide. 16 were bacteriologically positive.

The total dose required was only 14 grammes (28 tablets) for complete cure except in two cases with Shiga infection which required a little longer treatment. Almost all the patients were fit to resume work within five days. Stool culture was done up to three months with negative results in all cases. No relapse was seen up to a period of six months observation. The drug is found to be non toxic.

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

SOFIA F & CIARAVINO E. Inchiesta coprologica sui nativi dell Eritrea. [Faecal Examinations among Native Eritreans.] *Boll Soc Ital di Med e Igiene Trop* (Sez. Eritrea) 1944 v 4 Nos. 5-6 785-802. English summary (5 lines)

The authors have examined the faeces of 700 Eritreans in the Regina Elena Hospital Asmara. They discarded those with obvious intestinal disturbance in order to obtain a general idea of the degree of infestation among the people. They noted in each case the place of birth, changes of residence in recent years, occupation and any history of earlier intestinal disturbance but these points are not afterwards referred to in the record. The methods used were direct examination after a saline purgative and Willis's technique for helminthiasis and the Telemann enrichment method which gave much more satisfactory results.

The chief findings were *E. histolytica* in 209 (29.8 per cent.), *E. coli* 187 (26.7), *Trichomonas* 46 (6.5), *Chilomastix* 27 (3.8), *Giardia intestinalis* 15 (2.1). The figures for *E. histolytica* are compared with a selection of those recorded from time to time in other parts of the world, notably United States 11.6 (Craig), Brazil 9.3 (Pestana), Alexandria 13.7 (Wenyon & O'Connor), India and Mesopotamia 19.9 (MacAdam), Dutch Indies 24.0 (Brug), Jamaica 14.7 (Scott), Shanghai 10 (Fischer) and Venezuela 30 (De Bellard).

*Balantidium coli* was found once only. Of helminthic infestations the commonest was *Trichuris trichiura* 207 (29.5 per cent.) and next in order *Ascaris lumbricoides* 134 (19.1), *Ancylostoma duodenale* 132 (18.8). *Necator americanus* has been recorded by others but the authors did not meet with a single instance. *Taenia saginata* 58 (8.2), *Hymenolepis nana* 34 (4.8) and *Enterobius vermicularis* 24 (3.4). All these were diagnosed by finding the ova in the faeces. *Schistosoma mansoni* was found 6 times only (0.8 per cent.). Finally *Blastocystis* was seen in 21 (3 per cent.) H. Harold Scott

SHIH LU CHANG. Sedimentation in Water and the Specific Gravity of Cysts of *Entamoeba histolytica*. *Amer J Hyg* 1945 Mar v 41 No 2 156-63 2 figs. [10 refs.]

In a specially designed chamber (2×1.5×0.5 cm.) the rate of sedimentation of cysts of *E. histolytica* suspended in distilled water was directly followed by observation through a horizontally placed microscope. Readings were made with a micrometer eye piece. The sedimentation chamber was immersed during the observation in a mineral oil bath of uniform temperature in a larger glass chamber. The general result showed that in a sedimentation tank 10 feet deep at a temperature of 25°C cysts 15 microns in diameter would take approximately four days to settle. If water is subject to disturbances by wind or convection currents the settling time would be longer. Calculations by Stokes's law based on the settling rates, gave a specific gravity for cysts of

1-080. It seems evident that storage of water must be long if it is desired to remove cysts of *E. histolytica* by sedimentation. The paper (illustrated by diagrams) describes in detail the technique employed. C. M. Wexon.

MARUASHVILI G. M. On certain Differential Diagnostic Characters of Amoebic and Bacillary Dysentery *Med. Parazit. & Parazit. Dis.* Moscow 1944 v. 13 No. 6 57-62. [In Russian]

A description is given of supplementary methods for the differential diagnosis of amoebic and bacillary dysenteries. It was found that counts of neutrophils leucocytes with toxic granules in blood films proctoscopy and examination of the cell picture in the mucus, are of great help in cases when the usual methods of diagnosis fail. In bacillary dysentery the "toxic granules" are coarse, occurring in 53-88 per cent. of the neutrophils in acute cases dropping to 15-47 per cent. in convalescents. In amoebic dysentery the granules are fine and they are found in 11-35 per cent. of neutrophils subsequently falling to 8-18 per cent. Proctoscopic examination is regarded as a most important method for determining the form of dysentery according to the morphological changes undergone by the mucous membrane of the large intestine. While amoebic dysentery is characterized by numerous solitary circular ulcers with uneven margins and a coating of whitish-yellow mucus in bacillary dysentery the entire mucous membrane is involved. It is covered with layers of brownish mucus over large superficial ulcers which are circular or transverse. Further data are provided by examination of the mucus removed in the course of proctoscopy. This sometimes reveals the presence of amoebae microscopically or of dysentery bacilli in cultures even when these cannot be isolated from the stools. Finally much information can be obtained from the cell-picture of the mucus. In acute amoebic dysentery there are large numbers of neutrophils erythrocytes macrophages and epithelial cells but eosinophils are absent however in convalescent cases the last named elements increase progressively in numbers, while the other elements decrease. On the other hand in acute bacillary dysentery large numbers of pus cells erythrocytes and changed epithelial cells are present in addition to macrophages crystals of fatty acids and bacteria. In convalescent cases of this disease the number of red blood corpuscles and pus cells diminishes visibly while that of macrophages and epithelial cells increases, and solitary eosinophils begin to appear. C. A. Hoare.

CROPPER, C. F. J. Sigmoidoscopy in Amoebic Dysentery *Lancet.* 1945 Oct. 13 480-82.

The author who writes from India, points out that the disturbingly high incidence of chronic bowel disorders in those who have served in the East demands high competence in the handling of the dysenteries. He urges a more accurate study of the bowel lesions of amoebiasis.

Sigmoidoscopic examination is desirable for the diagnosis of chronic bowel disorders in patients who give a history of residence in an endemic area of amoebiasis in spite of the fact that the procedure has its limitations, and gives a negative result when there is active amoebic infection higher up.

It is not necessary in fresh, acute cases, in which diagnosis can be made by stool examination, but in other cases it may give much help. The symptoms of amoebiasis are so protean, that it is a precaution in—(1) Sprue (2) any case in which amoebic dysentery is suggested (3) refractory enteritis and headache (4) hepatomegaly and unexplained loss of weight. It should never be overlooked.

The ideal room for sigmoidoscopy should be situated at one end of the dysentery ward. If the examination is timed for 9.30 a.m. the following enemas should be given—7.30 a.m. half strength soap enema 8 a.m. 2½ per cent sodium bicarbonate enema. This procedure gives a very clean surface. No sedation is needed. The patient should be in the genupectoral or left lateral position and while the tube is being passed up the bowel attention should be concentrated on manipulation the detailed examination being carried out during the process of withdrawal of the sigmoidoscope. For identification of the lesions a lens giving a magnification of 4-5 diameters is essential.

The classical amoebic ulcers vary in size shape and distribution from small areas 1/3 inch in diameter to almost total ulceration of several inches of bowel. The unit of ulceration is the classical flat shallow depression with undermined, congested edges and of irregular diamond shape. There is a yellow purulent membrane with bright blood oozing scantily from its cracks and edges. There is no correlation between the duration of infection and the severity of the symptoms on the one hand, and the extent of ulceration on the other. These ulcers respond readily to emetine.

*Yellow-headed ulcers* are those in which bright shining homogeneous sloughs are present they may be widely scattered and may be separated by mucous membrane of normal appearance.

*Pin-point craters* are the commonest lesions found and may remain after the healing of the classical ulcers. The area in which they most usually occur is from 3 to 7 inches from the anus. They are seen as small dots surrounded by heaped edges their average diameter is 1-2 mm. The valves are often affected, and the whole visible bowel may be peppered with them giving the appearance of an aerial photograph of bomb craters on an airfield. These craters are not described in most standard works on amoebiasis but though definite evidence that they are amoebic in origin is difficult to obtain the author considers that they may justifiably be taken to indicate active amoebic infection. They are very refractory to treatment but may gradually disappear losing the central depression and resembling flat topped cutaneous warts. For demonstration of these craters it is essential so to manipulate the sigmoidoscope that the mucosa is illuminated obliquely. [Pin-point ulcers occur also in rectal schistosomiasis see this *Bulletin* 1945 v 42 47.]

*Pigskin appearance* is a term applied to minute scattered pits, resembling pin-pricks on the surface of Plasticine the pits are very persistent but may disappear. There can be little doubt of their amoebic origin.

P Manson-Bahr

SILVERMAN D N & LESLIE A Intractable Amoebic Colitis, with special reference to the Ulcero-necrotic Form. *J Amer Med Ass* 1945 Sept 15 v 129 No 3 187-90 3 figs.

The term *ulcero-necrotic* has excellent descriptive qualities but should be reserved for the type of case of which three are presented in this paper.

In the first two *E. histolytica* trophozoites were demonstrated in all layers of the colon from mucosa to serosa. In the third there was demonstrable extension to the submucosa. An unusual feature was the involvement of the entire colon in the ulcero-necrotic process which in the past has seldom been observed in America.

The first two were complicated by secondary infections with dysentery organisms Flexner in one and Duval (Sonne) in the other. It is possible, though not necessarily probable that this combination of pathological processes results in the diffuse ulcerating and necrotizing process which in one

case caused a major slough of the transverse colon and in the other a large mucosal slough of the recto-sigmoid.

Though the third case did not present the striking features of the other two the fact that the entire colonic mucosa was destroyed by the ulcerative process warrants its inclusion in the series. All these cases were fatal, and details of autopsy findings are given.

Case 1 ran a sudden and acute course of less than three weeks duration. The patient was febrile and severely ill. Six days after admission he passed a large tissue slough by rectum. The diagnosis was rupture of the ascending colon complete sloughing of the wall of the transverse colon intense ulceration of the whole colon suggestive of bacillary dysentery acute inflammatory hepatitis general peritonitis acute toxic splenitis and nephritis.

Case 2 had febrile diarrhoea with generalized abdominal pain for a year with exacerbation of one week.

The distal foot of the ileum showed occasional shallow ulceration. The wall of the colon was decidedly thickened, and except for an occasional patch of red oedematous mucosa, had been completely undermined by acute and long-standing chronic cellulitis.

Case 3 a man of 68 was undergoing radiotherapy treatment for carcinoma of the bladder. He had in addition a febrile bloody diarrhoea of two months duration.

The colon was adherent to the surrounding structures there were many areas of necrosis, but no area of complete perforation. The mucosa was destroyed by ulceration which involved the entire bowel, including the caecum and rectum. Many amoebae were seen in microscopic sections in the necrotic zones.

An increase in incidence of this type of case in the United States may be foreseen as a result of the local dissemination of amoebiasis, and the importation of virulent strains of amoebae from the oriental and tropical theatres of war

P. Manson-Baker

DE SILVA, S. "Significant Observations on Amoebic Hepatitis"—a Clinical Review of 200 Patients. *J. Ceylon Branch Brit. Med. Ass.* 1945 Apr., v 41 No 1 21-6 3 charts.

In the General Hospital, Colombo the number of cases of amoebic hepatitis liver abscess which averaged 88 in 1929 had swollen to 1,279 in 1944 the manifestations assumed so many different forms that they have afforded a rich field for investigation. In almost all cases the therapeutic test response to emetine injections supported the clinical diagnosis. In a series of 200 cases pathological confirmation was obtained in 60 and X-ray confirmation in 45.

About 70 per cent. were admitted with pain over the right lower chest this, together with sudden onset, high fever scanty crepitations and occasional pleuritic rub suggested pneumonia, and recourse was had to sulphapyridine therapy without success but directly emetine injections were substituted symptoms subsided. Previous and recent alcohol consumption is considered important. 178 patients confessed to excessive amounts over a period of 5-20 years, and it is suggested that alcohol may precipitate acute hepatitis in hitherto symptomless carriers. In 25 per cent. there was a history of vague abdominal pain, causing rigidity or guarding of the right rectus muscle and the amoebic splash in the right iliac fossa. Occasionally symptoms suggested an acute abdomen with appendicular colic—one with an anterior liver abscess simulated perforated gastric ulcer. A palpable epigastric tumour became apparent in 38.

In 68 the hepatic abscess was aspirated through the intercostal spaces but in 12 further operative interference became necessary in three a blood stained pleural effusion at first suggested carcinoma. Previous dysentery was recorded in 52 during a period of 3-5 years and the impression was obtained that a recent relapse determined the onset of hepatitis. In 12 the symptoms at first suggested haemorrhoids.

The pain of hepatic amoebiasis is dull especially noticeable on deep inspiration or on coughing causing the patient to incline to the left side. It is localized to the right lower intercostal spaces over the area occupied by the liver. Pain referred to the right shoulder or neck in 44 constituted a prominent symptom. Hepatitis pain is never referred to the lower abdomen as may happen in basal pneumonia or pleurisy. It is intensified at night aggravated by alcohol by deep breathing and increased by percussion.

The increasing numbers of hepatitis cases are attributed to incomplete treatment of amoebic dysentery.

P Manson-Bahr

SPADARO O. *Lepatite amebica (studio clinico)* [Clinical Study of Amoebic Hepatitis.] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Ser. Entrea) 1944 v. 4 Nos. 5-6 825-47 5 figs. [105 refs.] English summary (8 lines)

The author's statements are based on 50 patients treated in the Regina Elena Hospital Asmara during the 5 years 1939-44. Forty were Europeans and 10 were Eritreans. Each year an average of 216 cases of intestinal amoebiasis has been found by microscopic examination and this is below the real amount of infection for statistics show that 29.8 per cent. of presumably healthy subjects yield positive findings of *E. histolytica* in their faeces [see SOFIA and CLARAVINO above]. In this connexion it is worth noting that of the 50 referred to in the present paper only 24 had given any history of an earlier enterocolitis and 21 were passing amoebae in their stools. Nine of the series, who had actual liver abscess and entamoebae in the stools, declared that they had never suffered from diarrhoeal attacks of any note and 16 patients (12 of them Europeans) had never had any intestinal disturbance of any importance although the entamoeba was present in their stools.

Nine of the 50 died they had for long had enlarged livers. In 48 the abscess was in the right lobe. Early symptoms were debility dyspepsia and enlargement of the liver with fever. Anorexia nausea and vomiting were often but by no means always present the same applies to shivering attacks and sweating. Subicterus was present in 10 true jaundice in three only. Pain may be very acute and limited to the lower border of the liver in others it may be more intense in the 9th and 10th intercostal spaces in the axillary line. Right-sided basal pleurisy was not infrequent. Leucocytosis was not very marked up to 16 000 per cmm. in colliquative hepatitis. Radiology is of great help in diagnosis a marked feature being immobility or restriction of movement of the diaphragm on the affected side with enlargement of the liver. The chief complications are secondary infection spread of the abscess and opening into the lung. Prognosis depends much on whether the abscess is single or multiple. OCHSNER's figures are quoted of 100 per cent. fatality in multiple cases and 10.5 per cent. in unilocular abscess. Another important point in prognosis is the treatment adopted. In the old days of ipecacuanha the fatality rate was about 12 per cent. after emetine came into common use it was from 2.6 to nil. DOMINICI in Italy had a rate of 0.8 per cent. among 114 cases [one death presumably]. Other figures quoted are 38 cases with medical treatment and hepatocentesis 5.26 per cent. 38 with surgical and medical treatment combined 28.42 per cent. 17 with surgical treatment alone 29.92 per cent.



The author's patients have been treated with emetine 90 cgm. in all three injections are given daily each of 3 cgm. after 45 cgm. have been given (5 days) an interval of 10 days is allowed to elapse during which stavarsol or yatren is given. In the colliquative forms the emetine treatment is combined with evacuation of the abscess cavity and washing out with a solution of emetine. Good results have followed collapse therapy of the abscess cavity by means of Potain's aspirator. Cures have been attained in 20 days in this way but emetine treatment has been maintained by a course every three months for about a year. Details of six cases are given in an appendix.

H. Harold Scott.

PICARD H. & BEN-SIMON T. Skin Amoebiasis. *Acta Med Orientalis (Palestina & Near East Med J)* 1945 Aug v 4 No 8 282-4

Amoebiasis of the skin is easily diagnosed if suspected but is often unrecognized. It is almost certainly fatal if specific treatment is not given but treatment with emetine is effective.

It is probably not extremely rare as 74 proved and 28 suspected cases were reported in 1940. In the present paper the authors record 7 cases in 5 of which [4 according to the text] *E. histolytica* was found. The areas of skin affected were at the incision for operation for liver abscess (1) at the incision for appendicectomy (2) and the perianal skin (1).

The authors think that a debilitated state of health increased virulence of the amoebae and perhaps the presence of other infections may be contributory causes.

Treatment is by emetine injections in very rare cases where this may fail, wide excision of the area may be required.

J. F. Corson.

CLARKE J. B. Amoebic Infection of the Vulva complicating Granuloma Perianth. *J Trop Med & Hyg* 1944 Oct-Nov. v 47 No. 5 54-5.

KERN F. Jr. Amoebic Pericarditis. *Arch. Intern. Med* 1945 Aug v 76 No. 2, 88-92, 2 figs.

"In a case of amoebic pericarditis subsequent to extension of an amoebic abscess of the liver the clinical impression was that of tuberculous pericarditis and the diagnosis was established only at autopsy."

EDINGTON A. D. A Simple and Practical Method of treating Amoebiasis. *South African Med J* 1945 Aug 25 v 19 No. 16 294

The treatment recommended in this paper is presumably intended for cases of chronic amoebiasis of the intestine as it does not prevent the patient from doing his daily work. Emetine bismuth iodide is given in 3-grain doses on an empty stomach early in the morning accompanied by a drink of half a tumblerful of ice-cold water. The patient at once lies on his right side and remains so for an hour. This dose is given daily for 10 days. The course is followed by a carb[er]ionic treatment of 20 tablets which are taken twice a day [0.25 gm. *bis die* for 10 days?] and if the patient finds HCl does not induce dyspepsia or heartburn he takes 5-15 drops in a large drink of water after each meal.

The author treated 107 patients suffering from amoebiasis and most of them were able to enjoy their breakfast during the course. A few vomited once or twice and in some the drug caused mild diarrhoea, but all completed the course. At the end of treatment only two patients showed a few cysts and only one had any toxic effects—mild sciatic pains in the legs. No relapses have occurred in the cases followed up.

The gastric juice was examined in 67 cases of amoebiasis the great majority of these patients had hypochlorhydria and several had achlorhydria while only two had ' a very slight degree of hyperchlorhydria. J F Corson

PESSÔA S B & AMARAL, D F Ação da emetina sobre a *Entamoeba histolytica* em cultura como teste do seu valor amoebicida. [Action of Emetine on *Entamoeba histolytica* in Culture as Test of its Amoebicidal Value] *Brasil Medico* 1945 July 7 & 14 v 59 Nos 27 & 28 241-4 English summary

The authors have found that *E. histolytica* will grow well in a medium consisting of a solid base of coagulated ox serum covered with Locke's solution to which a quantity of defibrinated ox blood has been added. The amoebicidal action of emetine and cephalin were tested by adding solutions of various strengths to cultures maintained at a pH of 7.4 to 7.6 and at a temperature of 37.5°C. It was found that emetine was amoebicidal and hindered growth when the concentration in the medium was 1 in 20 000 while cephalin ceased to be amoebicidal at a dilution of one in 10 000. The action of cephalin was not altered by boiling or autoclaving the solution before testing it.

C M Wenyon

AMIN N MAHFOUZ M & SHERIF M A F The Pharmacological Action of Quassin as compared with Emetine *Quart J Pharm & Pharmacol* 1945 Apr-June v 18 No 2 116-21 4 figs.

The author has made a pharmacological study of quassin and compared it with emetine hydrochloride with special regard to its action in causing depression of the heart and a lowering of the blood pressure. He has also studied the action on cilia of the toad's buccal membrane trichomonas from the caecum of guinea-pigs and *Entamoeba histolytica* from cases of amoebic dysentery. In all these tests quassin was superior to emetine. It proved to be non-toxic to animals in large doses and only depressed the heart and lowered the blood pressure in high concentrations. It was also more effective than emetine in its action on the cilia and the protozoa. Quassin was accordingly tried by intramuscular injection in certain cases of acute amoebic dysentery and the results are said to have been encouraging. [It seems exceedingly doubtful if *in vitro* observations on amoebae and trichomonas while in faeces justify conclusions as to the relative activity of the substances tested.]

C M Wenyon

LÄNG S Ueber die intravenöse Urotropinbehandlung der Lambhia-Cholecystitis. [Treatment of Giardiasis Infection by Intravenous Injections of Urotropin.] *Schweiz med Woch* 1945 Aug 4 v 75 No 31 679-80

The author discusses the various views that have been held regarding the pathogenicity of *Giardia* particularly from the point of view of cholecystitis. He notes that some observers consider the main habitat of the flagellate to be the duodenum while others hold that the gall bladder is the main seat of infection. Observers are fairly well agreed that when samples of bile are withdrawn by duodenal tubage it is in the B fraction that the greatest number of *Giardia* are found while it has been claimed that in three cases in which the gall bladder had been removed for cholecystitis the flagellates had been found in the bile inside this organ. Furthermore it has been observed that treatment with bismuth or stovarsol will cause the *Giardia* to disappear from the duodenum for some days but they reappear presumably because these drugs have no action on the contents of the gall bladder. The author admits however that other observer

have failed entirely to find the flagellates in gall bladders removed for so-called *Giardia* cholecystitis. He favours the view that symptoms of cholecystitis are due to invasion of the gall bladder and he is supported in this conclusion by his observation that in a number of cases intravenous injections of urotropine which is known to be excreted in the bile have brought about not only an eradication of the infection but complete relief from all symptoms. The treatment has consisted in the daily intravenous injection of 10 cc. of a 40 per cent. solution of the drug for four to six days. The action of the drug was controlled by duodenal tubage.

C. M. Wesson

## RELAPSING FEVER AND OTHER SPIROCHAETOSIS

STUART G. Relapsing Fever in North Africa and Europe, 1943-1945. *Epidemiological Information Bull* (UNRRA Health Division) Washington D.C. 1945 July 15 v 1 No. 11 453-64

The author refers to the epidemic of louse-borne relapsing fever recently present in Tunisia, Algeria and Morocco and gives a historical survey of outbreaks in that area and in other French African possessions since 1919. The present epidemic probably originated in Fezzan and began in Tunisia in September 1943. In 18 months there were 30 744 cases in Tunisia alone, and during the latter part of 1944 and the early part of 1945 there were 5 062 cases in Algeria and 667 in Morocco. The epidemic was still raging according to the last available returns, in February-March 1945.

In Tunisia the disease was at first mild, but as the epidemic extended, severity increased and the case mortality rate reached 10-12 per cent.

In Europe 578 cases of tick-borne relapsing fever were reported in 1943-44 from Spain and the louse-borne form has recently been recorded from Turkey, Rumania, N. Ireland and England. In Greece and France there have also been cases, the latter in maritime areas having connections with N. Africa. The tick-borne form is not uncommon in Tunisia where *Ornithodoros erraticus* is widely distributed and where *O. savignyi* (a potential vector) is found towards the south. *Rhipicephalus sanguineus* also a potential vector is found in Algeria.

Three recognised carriers of the disease have been recorded from Libya, viz. *O. moubata*, *O. savignyi* and *O. laborensis* [presumably *O. laborensis*]. It is said that tick-borne relapsing fever occurs there.

In the French experience of louse-borne relapsing fever stavarsol was ineffective but with novarsenobenzol or mapharsen the results were very good. The optimum doses for an adult weighting 60-85 kgm. were —

Novarsenobenzol — 0.6 gm. the first day 0.75 gm. the following day and one stimulating dose a week later.

Mapharsen — 0.06 gm. the first day and the same the following day.

Charles Wilcocks.

WOOD R. C. & DRYAN K. C. Tick-borne Relapsing Fever in Cyprus. *Brit. Med. J.* 1945 Oct 20 526-8 1 fig

The authors noticed that cases of relapsing fever were occurring in Cyprus among soldiers who had passed the night in caves or dungeons. A careful search of caves where infection had occurred revealed the presence of *Ornithodoros tholozani*, a known vector of relapsing fever which has not previously been recorded in Cyprus.

Twelve cases are described in detail. No lice were found on any of these patients, and in all cases there was either direct or indirect evidence of exposure

to the bites of ticks. The incubation period was usually 8 to 10 days. In two cases long periods of low continuous fever occurred as well as acute attacks of high pyrexia. Choroiditis was seen in one case and papillitis in four others. No other neurological complications were noted except changes in the cerebrospinal fluid. The urine was examined for urobilin in seven cases and marked urobilinuria found in six of them. All the cases were treated by intravenous arsenicals five relapsed but only two more than once.

In an appendix one of the authors K C D records that he had succeeded in infecting guinea pigs by the inoculation of blood from another case of relapsing fever in Cyprus. This supports the view that the causative organism is *Spirochaeta hispanica* the tick borne strain of relapsing fever spirochaete which is found in other Mediterranean countries. E Hundle

MARUASHVILI G M [On the Tick-borne Relapsing Fever] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 1 24-7 [In Russian]

This paper deals with the occurrence in the Caucasus of tick-borne relapsing fever which was first noted there in 1928 since when only a few cases have been recorded. The disease is caused by *Spirochaeta caucasica* and is transmitted by *Ornithodoros verrucosus* which is found exclusively in burrows and caves inhabited by wild rodents (*Pallasimus* [*Pallasomys*?] *erythronus caucasica* [= *Meriones erythronus caucasicus*?] *Apodemus sibiricus* and *Mus musculus*) representing the reservoir hosts of the infection. Man becomes infected only when coming into contact with these biotopes [habitats]. The author records his observations on seven patients who were admitted to an evacuation hospital with a mistaken diagnosis of malaria. The incubation period is 6-10 days the onset of the first paroxysm of fever is sudden and it lasts 2-4 days with a temperature up to 39-41°C. The subsequent paroxysms are usually of short duration lasting up to 10 hours and terminating abruptly with copious perspiration. These paroxysms may at first recur every other day or every third day resembling benign tertian and quartan malaria, but later the apyrexial intervals gradually increase in length sometimes lasting more than one month. The number of relapses may reach 12-15 the duration of the disease being up to 3 months. Among other symptoms the author notes a transient functional cardiovascular insufficiency, nausea and even vomiting during the first paroxysms of fever. The reaction on the part of the spleen and liver is very slight and there are no characteristic changes in the blood picture.

In the early phases of the disease Caucasian tick relapsing fever can be confused with malaria. Its differential diagnosis is based on the finding of spirochaetes in the blood of the patient or in experimentally infected hamsters. The disease was treated successfully with osarsol in doses of 0.25 gm given three times a day during 3-5 weeks. C A Hoare

## YAWS

TOMPSETT R. R. & KAUER G L. Penicillin Treatment of Early Yaws. *Amer J Trop Med* 1945 May v 25 No 3 275-6

Five cases of yaws in Melanesians of the New Guinea area were treated with penicillin. One patient was given 250 000 units in doses of 25 000 units intramuscularly every 4 hours while the other four each received 400 000 units in doses of 20 000 intramuscularly five times daily at intervals of 4 hours.

Spirochaetes could no longer be found 15 to 24 hours after the beginning of this treatment and the lesions healed within 3 weeks. The Kahn reaction remained positive during the few weeks of observation but could not be observed longer as the patients disappeared when the lesions were healed.

J. F. Corron

GUDMARÆS F. N. Penicilina e bouba (Framboesia, Pian Yaws) Dose curativa minima. Redução do número de injeções diárias. Redução do tempo de tratamento pelo aumento das doses. (Nota prévia.) [Penicillin and Yaws.] *Brasil Medico* 1945 June 16 23 & 30 v 59 Nov. 24 25 & 28 221-4 6 figs. English summary

This is a short article published as a preliminary note but it considers several points of importance as shown in the subtitle the minimal curative dose, the results of using smaller doses or of using larger doses over a shorter period. Experimentally spirochaetes in animals had proved to be very susceptible to the action of penicillin so it was decided to test its action in human spirochaetoses.

First with doses of 150 or even 100 Oxford units intramuscularly administered every four hours clinical cure was obtained in 17 days the former with a total dosage of 15,300 units in a girl of 9 years the latter with 10,300 units in a girl of 10 years. Another child of 10 years was given 50 units every 4 hours over a period of 40 days (12,000 units in all) but without obtaining clinical cure.

Next tests were made to ascertain the results of reducing the number of daily injections. With doses of 400 units three times a day cure was obtained in 14-16 days i.e. with a total dosage of 16,800 and 19,200 units. With two injections daily each of 400 units clinical cure resulted in a child of 2 years after 16 days treatment and in one of 11 years after 23 days treatment. To two children a single daily dose was given one, a girl of 9 years received 3,200 units daily and was cured in 20 days. The other was the boy who had failed to respond to the 50 units every 4 hours after 40 days (see above). He was given a single dose of 1,600 units daily for 30 days (total 48,000 units) and was cured.

All the patients referred to above were children—the oldest was 11 years of age for adults the author states that these doses should be doubled.

Thirdly the trial of increasing the doses and reducing the period of administration was made. The dosage was graded according to the body weight. To a youth of 16 years weighing 42 kilos a dose of 46.7 units per kilo was given every 4 hours and cure was obtained in 15 days the same occurred in children of 4 to 12 years with doses of 33.3 units per kilo every 4 hours. It is to be noted that in none of these three were any spirochaetes seen in the lesions 72 hours after the treatment was started, but it was continued nevertheless for several days to consolidate the cure and to obtain reversal of the Wassermann reaction

H. Harold Scott

## LEPROSY

MARIANO J. Pênfigo bolho-esfoliativo e lepra. [Exfoliative Pemphigus and Leprosy.] *Rev. Brasileira Leprológica* S. Paulo. 1945 June v 13 No 2, 103-6 2 figs.

A leper woman of 42 years clinical type N1 developed a bullous rash on the thorax which was at one time thought to be pemphigus foliaceus but the

bullae were associated with ulcerating and scabbing areas. 'The type and localization of the lesions by themselves rule out the possibility of Dühring's disease' says the author [but dermatitis herpetiformis commonly occurs on the trunk]  
H Harold Scott

CAMPOS N S & SOUZA P R. *Lepra e sífilis* *Leprides sífilóides o sífilides lepróides*. [Leprosy and Syphilis.] *Rev Brasileira Leprologia* S Paulo 1945 June \ 13 No 2 77-94 17 figs.

This paper deals with an important and puzzling question—the resemblance between certain lesions in leprosy and those in syphilis. Lesions may bear so strong a resemblance to each other—syphilis-like leprides and lepra like syphilides—that a wrong diagnosis is likely to occur and valuable time be lost before the appropriate treatment is undertaken.

The similarities are duly shown by the authors, notably the roseolar exanthem of leprosy to that of syphilitic roseola, tuberculoid leprosy to certain late secondaries in syphilis. Distinctions on paper at least are not easily recognized, being matters of degree rather than of kind. Thus in roseolar exanthemata of leprosy the patches are larger than in syphilis and in the latter they are more homogeneous and equal in size and evolve more rapidly. As for the tuberculoid lesions they are less polymorphic in leprosy than in syphilis and their development is slower taking 6 to 12 months. The Wassermann reaction may help especially if negative but it may be positive in some lepers. The clinching diagnostic point is the finding of the organism by biopsy.

Excellent photographs illustrate the paper but it must be confessed (by the abstractor at least) that they afford less enlightenment than one hoped. They bear appropriate legends otherwise it would be difficult to distinguish for example Fig 1 a tuberculoid leprosy from Fig 13 a late secondary syphilide. Cases of papulo-tubercular syphilis simulate it will be seen to an extraordinary degree instances of severe facial lepromata. To one photograph depicting the histological changes in a syphilitic is the legend granulation of tuberculoid structure indistinguishable histologically from that met with in tuberculoid leprosy.  
H Harold Scott

LIMA L de S & CERQUEIRA, G de C. *Terapêutica experimental da lepra pela solutiazamida*. [Treatment of Leprosy with "Solutiazamide"] *Rev Brasileira Leprologia* S Paulo 1945 June \ 13 No 2 97-100

Solutiazamide is stated to be p (γ phenyl propyl amino) phenyl sulphamidothiazole x γ-disulphonate of sodium and prepared directly from sulphathiazole and is very readily soluble in water. A solution of 45.3 per cent. corresponds to a 20 per cent. sulphathiazole base. It was administered daily (except Sundays) intravenously in doses starting with 1 cc. and increasing up to 5 cc. or for adults 10 cc. After three weeks an interval of one week is allowed to elapse before the treatment is continued. The treatment is controlled by a blood count and haemoglobin estimation every 10 days, examination of the urine and any deposit, and an estimation of the drug in the blood. If the red cells fall below 3½ million per cmm. the dose of the drug is reduced and liver preparations are given. The urine is examined for blood and albumin or any indication of nephrosis and if it appears treatment is suspended.

The new drug was tried in 50 cases of moderately developed lepromatous forms and others more advanced. 50 cases of lepromata with skin involvement and lesions of eyes and nose and some in whom chaulmoogra had been tried ineffectually. The authors publish their results in order that others may be led to make trial of the drug. So far reported these results sound almost too

good to be true. The authors report rapid cicatrization of leprosy ulcers, cicatrization of fusing lepromata, disappearance of lepromatous infiltrations to the level of the skin, softening and disappearance of cutaneous nodules perforating ulcers are sometimes benefited the ocular lesions improve and do not relapse, nasal crusts disappear obstruction is relieved and dyspnoea subsides.

H. Harold Scott.

### HELMINTHIASIS.

SHUMIKO, A. I. On the Degree of Infestation of Vegetables and Fruit with the Eggs of Helminths in Samarkand. *Med. Parazit. & Parazit. Dis. Moscow* 1944 v 13 No 6 77-8. [In Russian.]

The author describes the results of examination of vegetables and fruit from the bazaars of Samarkand for the presence of eggs of helminths. Investigations were made at different periods in 1937/8 and 1942/3 using the following method. Each portion to be examined was carefully washed twice by hand in 500 cc. of tap-water (total volume of water=1 litre). The water was then passed through a metal sieve (diameter 2 mm.) into a vessel in which the height of the water varied from 6 to 15 cm. The washings were allowed to settle for 2-3 days or longer after which the water was siphoned off and the deposit poured out into centrifuge tubes (1-2 cm. per tube). After centrifugation for 3 minutes the supernatant water was decanted, Darling's reagent was added to the tube the contents were carefully mixed with a glass rod, and centrifuged again for 3 minutes. The surface film was then removed with a metal loop and examined under the microscope. The total number of samples of vegetables thus examined was 210 in which were found 44 oncospheres of tapeworms and four threadworm eggs.

C. A. Hoare

HOOG, E. H. V. Intestinal Infestations. *Practitioner* 1945 Nov v 155 No. 5 306-12. [27 refs.]

A summary of recent work

BLACK, K. O. Cutaneous Schistosomiasis Involving *S. haematobium* Eggs. *Brit. Med. J.* 1945 Oct 6 453-6 3 figs.

This interesting paper records the occurrence of bilharzial skin lesions on the trunk of certainly two and probably four of 130 male Europeans harbouring *S. haematobium*. All four cases were presumably heavily infected with the parasites as they had been repeatedly exposed to cercarial attack over a period of a month or more in West Africa. Each experienced skin sensations and developed skin lesions at the time of infection and each went through the classical febrile reactive stage of bilharziasis before ova appeared in the stools some three months after the initial infection. In only three of the four cases did ova subsequently also appear in the urine.

*Case I*—On being specifically diagnosed was promptly treated with 40 cc. of stilbophen intramuscularly over a period of 15 days. On the seventh day of treatment he drew attention to some herpetiform lesions in the skin below the right nipple. Shotty papular lesions then developed on the lower chest upper abdomen, lower back upper buttock, scrotum and perineum. Repeated aspirations of the lesions yielded *S. haematobium* eggs on many occasions.

*Case II*—On diagnosis by stool examination was also immediately treated with stilbophen. Again, one week after starting treatment, papular lesions were

noticed in this case in the left lumbar region. Similar lesions appeared on the lower left chest and these on aspiration yielded *S. haematobium* ova. Four further clusters of lesions and some scattered isolated papules developed in the left lumbar, the sacral and gluteal regions in this case.

Case III was a mixed *S. mansoni* and *S. haematobium* infection with two similar clusters of papules in the lumbar region but ova were not recovered from these.

Case IV was also a *S. haematobium* infection, with a group of spots to the right of the umbilicus but here again ova were not recovered from the lesions.

Owing to the similarity of the skin manifestations in all four cases it is reasonable to assume that all were of similar origin.

The author in discussing the matter points out the similarity at some stages of the skin lesions he describes to those seen in the bladder or the bowel on endoscopy and he believes they resemble the cutaneous manifestations described by MADDEN [this *Bulletin* 1919 v 14 339] and by GIBGES [*ibid* 1934 v 31 907]. In his own cases however the lesions did not go on to the ulceration and sinus formation described by these authors. He speculates on the route by which the worms depositing the causative ova reached the site of their recovery in the skin and suggests that they may have ascended the scrotal, gluteal and lumbar veins from the iliac veins and vena cava, or travelled by the venous communications between the lumbar and epigastric veins or by the inferior epigastric from the external iliac veins. Some of the recovered eggs were dead and degenerate others were healthy and viable.

A. R. D. Adams

MILLER, S. E. *Schistosoma Haematobium* Infection. *J Amer Med Ass* 1945 Sept. 29 v 129 No. 5 344-7 5 figs.

Report of a case

MARIANI TOSATTI G. Bilharziosi intestinale da Sch. Mansoni in Eritrea. Descrizione clinico-anatomo istologica. [*Schistosomiasis mansoni* in Eritrea.] *Boll Soc Ital di Med e Igiene Trop* (Sez. Eritrea) 1944 v 4 Nos. 5/6 803-13

In 1936 Dr SATTA noted and recorded the presence of *Schistosoma mansoni* in the higher levels of Eritrea [this *Bulletin* 1936 v 33 553 953]. The author remarks that Clayton LANE maintained that this schistosomiasis was absent from Eritrea. [This is a mistake which the present author should not have made. Lane had stated (*ibid* p 11) as regards Eritrea, 'no accounts have come to light' and this as Lane maintained (p 953) is very different from affirming that the infestation is non-existent.] Three new cases are here recorded, two from the neighbourhood of the original focus in the Marazzanu Concession, the third from near the village of Toselli 4 kilometres from Decameré. All three were in children 10 years old. The first two had bathed in the same stream, had felt intense itching of the legs and later suffered from fever, urticaria, and muco-sanguineous diarrhoea with abdominal pains. The symptoms persisted for some months but after coming to hospital, the patients were treated with Fouadin and made good recoveries. The third child bathed in a brook near his home. He felt severe itching especially on the legs and 10 days later had a very irritating diffuse red rash and, a few days after diarrhoea with four to six motions daily containing mucus and blood. He had previously suffered from taeniasis and he passed some proglottides. He was now treated for this last with satisfactory result. He seemed better for 3 weeks or so but then became rapidly worse with malaise, shivering, intermittent fever and muco-sanguineous diarrhoea within the next fortnight he



became pale, lost weight and suffered from an irritating cough and shortness of breath, was admitted to hospital (three months after the incriminated bathing) and he died a fortnight later. At autopsy, the lungs showed nodular infiltrations containing ova of the schistosome, as did also the peritoneum. The general structure of the liver was retained but the central parts of the lobules showed intercellular oedema, the Kupffer cells were increased in number and were stuffed with black granules. In the sinusoids were small-cell infiltrations and there was general biliary cirrhosis. The spleen showed marked increase in the reticular tissue and some increase in the trabecular connective tissue. The organ was enlarged and weighed 300 gm. The intestine had a much thickened mucosa, stuffed with ova "about 60 per field" & few were present also in the muscular layers. The kidneys revealed nothing particular to note.

H. Harold Scott

KHALIL BEY M. HALAWANI, A. & GAMAL NOR EL DEEN. The Problem of Post-Antimony Jaundice in Egypt. *J Roy Egyptian Med Ass.* 1945 *xxv* v 28, No. 5 192-208. [13 refs.]

Following the mass treatment of the population in one district in Egypt for bilharziasis with two trivalent antimony compounds, jaundice occurred in a number of patients. About 3 per cent. were affected in 8,000 cases treated with tartar emetic given intravenously while there was only one case of jaundice among 2,000 cases treated intramuscularly with stibophen. The jaundice occurred 1-3 months after treatment the greatest incidence being at the end of the longer period. The condition was accompanied by slight fever and certain constitutional disturbances among which gastro-intestinal symptoms were marked, and the period of upset lasted several weeks. Clinically the cases resembled those due to infective hepatitis but the incubation period was longer. It was later found that jaundice has occurred in some communities in the absence of antimony treatment. The presence of infective material in imperfectly sterilized syringes was therefore suspected, and this view appeared to be confirmed when adequate measures for their sterilization were introduced.

J. D. Fulton.

SOTOLONGA, F. ALFONSO J. & DEL VALLE ALEMÁN S. Inermicapsiferosis. Revisión general en ocasión del estudio de un caso procedente de Santa María del Rosario [Inermicapsifer Infestation. A General Account and Report of a Case. *Rev. Med. Trop. y Parasit. Habana.* 1945 May-June-July-Aug. v 11 No. 3 & 4 37-40]

LAPTEV, A. A. [Strongyloidiasis of the Lungs.] *Klinicheskaja Meditsina* Moscow 1945 v 23 No 3 75-6. [In Russian.]

The author describes a subject infested with *Strongyloides* [the species is not stated] in whom the symptoms were pulmonary intestinal symptoms being absent. Larvae of *Strongyloides* were found in the sputum only.

The subject was a Moscow carpenter aged 34 who had not left that city. At first he suffered from sharp attacks of dyspnoea with slight cough and expectoration of small quantities of odourless muco-purulent sputum which was free from blood. His temperature was 37.8 to 38.3°C. A slightly-itching urticaria appeared over the whole body followed by oedema of the face and lower extremities both these lasted only 24 hours. The next day the subject's condition was serious. In hospital a general examination revealed little except bubbly râles in the right scapular region and, by X-ray, a diffuse, inconspicuous darkening of the whole right pulmonary field, especially in the region of the right scapula. Right-sided bronchopneumonia was diagnosed.

There was an eosinophilia of 22.5 per cent. Neither *Strongyloides* nor its eggs were found in the faeces but freely moving mature *Strongyloides* were found in the sputum. On the sixth day after admission to hospital 3-20 specimens per preparation were found but three days later there were only isolated specimens. Two days later still neither *Strongyloides* nor its larvae could be found in the sputum.

The bronchopneumonia was treated with 1.0 [presumably gm] of sulphidino [sulphapyridine] four times daily but the subject's condition continued to be grave the high eosinophilia remained and some 50 cc. of sputum were voided in 24 hours. More careful examination of this sputum revealed mature *Strongyloides* in it. The subject was then given 20 cc. of 33 per cent alcohol intravenously and simultaneously 0.1 [presumably gm] of methylene blue by the mouth in gelatine capsules. After three such doses of alcohol the dyspnoea decreased the sputum came away freely the cough improved and the temperature became normal. In the sputum only isolated *Strongyloides* were found and after eight doses of alcohol they completely disappeared. A total of 20 such doses of alcohol was given. The methylene blue was continued for 15 days. Eventually the X-ray picture of the lungs became normal. *Strongyloides* could not be found in the sputum and the subject was discharged in very good condition.

The author remarks that *in vitro* extract of male fern kills larvae of *Strongyloides* in 10 minutes. After mentioning various remedies for strongyloidiasis the author refers to Faust's opinion that gentian violet has a specific action on *Strongyloides* [cf. CRAIG and FAUST *Clinical Parasitology* 3rd edn. 1943 p. 253 London: Henry Kimpton] where intravenous administration of not more than 25 cc. of 0.5 per cent aqueous solution of gentian violet on alternate days for not longer than ten days is recommended for pulmonary infestation with *Strongyloides*.  
G. Lapage

HILLY I. S. The Effect of the Flooding Method of Sewage Disposal on the Viability of the Eggs of *Ascaris lumbricoides*. *J. Roy. Egyptian Med. Ass.* 1945 May v 28 No 6 207-14.

The health authorities at Cairo are concerned as to the possibility of disease being spread from the use of human excreta for fertilizing purposes. Biological treatment of sewage will destroy pathogenic organisms but the question of the survival of *Ascaris* ova is another matter since this ovum is one of the most resistant of all helminthic ova and the worms are very fertile. Before the

Flooding method of dealing with sewage was introduced these ova would survive without much difficulty. Now the following is the procedure. Liquid sludge and scum from sedimentation tanks are pumped on to drying beds each of an area of 49 sq. metres and spread as a thin layer and left to dry for 5 days in summer 8 days in early spring and late autumn. Then another layer is applied and so on till as many as 20 layers may have been deposited. It is then covered with half an inch of sand and flooded with sedimented sewage and left for a fortnight then turned over and in 2-3 days (in summer) the whole is dry enough to distribute as manure. Thus about three months are needed for the whole process.

Examinations for viable ova of *Ascaris lumbricoides* were made after the four 3-monthly periods. Briefly stated, the results were that no viable eggs were found in samples from the beds prepared from March-June, June-September and September-December but they were present in those prepared in the remaining quarter December-March after 10 days storage. After 25 days storage by the ordinary piling method in this last period viable eggs were still

present but not after 30 days storage. The latter is therefore more economical for the December-March period and this is fortunately not the fly-breeding season the Flooding method is best for the rest of the year. It is not only a good method of sewage disposal but the fertilizer resulting therefrom is safe and free from viable eggs of *Ascaris*.  
H Harold Scott

NEWTON W L, WRIGHT W H. & PRATT I. Experiments to determine Potential Mosquito Vectors of *Wuchereria bancrofti* in the Continental United States. *Amer J Trop Med* 1945 May v 25 No 3 253-61 [12 refs.]

As many American soldiers and sailors have returned to the United States suffering from filariasis the authors made experiments to see whether mosquitoes in the United States could transmit the infection the experiments were begun in Porto Rico with species of mosquitoes common to that island and to the United States and later were continued in Alabama.

Between July 1943 and October 1944 a total of 2,371 mosquitoes, comprising 16 species, fed on infected volunteers a short description of the feeding peculiarities of each species is given. After various intervals, beginning 9½ days after feeding, the mosquitoes were killed and dissected the wings and legs were removed and the mosquito was divided into abdomen thorax and head and these parts were teased in normal saline under the dissecting microscope.

The development of the microfilariae corresponded with the textbook descriptions in most of the species in which full development took place it was complete within two weeks.

Altogether 1,801 dissections of 15 species and 49 of *Culex tarsalis* were made the former being shown in a table the latter being added in a postscript. The results indicated that *Culex quinquefasciatus* [*C fatigans*] *Culex tarsalis* *Psorophora confinis* and *Anopheles albimanus* would be excellent vectors in favourable conditions. *Culex nigripes* *Aedes aegypti* and *Aedes triseriatus* could convey the infection, but their low infectivity rates in this experiment suggest that they could not be important vectors. *Aedes sollicitans* *Aedes taeniorhynchus* *Aedes vexans* and *Anopheles punctipennis* could not apparently transmit the infection. The results with *Anopheles quadrimaculatus* *Culex erraticus* *Culex salinarius* *Psorophora ciliata* and *Psorophora discolor* were inconclusive.

The potential infectivity rate of *Psorophora confinis* of the United States was 80 per cent. while in the apparently identical mosquito of Porto Rico it was only 12 per cent. 104 mosquitoes of each race having been dissected the two groups of strains of this species were apparently physiologically different.

J F Corson.

NEWTON W L. & PRATT I. Experiments to determine whether Infective Larvae of *Wuchereria bancrofti* can migrate from the Abdomen of the Mosquito Intermediate Host. *J Parasitology* 1945 Aug v 31 No. 4 268-8.

The mosquito's legs and wings were removed, then a longitudinal incision was made along the lateral abdominal wall and a drop of saline containing from 1 to 7 infective larvae of *Wuchereria bancrofti* was placed on the incision the larvae entered the abdomen and the incision became closed within a few minutes. After about an hour the mosquito was divided into abdomen, thorax, head and proboscis and these parts were examined for the presence of larvae.

Migration was found to have taken place in 22 of 27 mosquitoes of 68 active larvae recovered, 32 were in the thorax, 12 in the head or proboscis and 24 in the abdomen. The time of migration varied greatly in one case a larva had reached the proboscis within 5 minutes while in another case it took 105 minutes.



naval hospitals and convalescent centres. The Marine Barracks had hospital wards and laboratories and the staff included medical specialists laboratory research workers and technicians nurses and corporals.

In many cases, partly owing to their previous sedentary or convalescent life there was a good deal of hypochondriasis with psychosomatic reactions in the course of time however and when the incurable psychoneurotics were removed, the general mental attitude of the men improved greatly. Two groups were compared those with signs or a history of recent filariasis and those who had returned to America 6 to 12 months previously and had been in hospital the former returned to active duty more easily than the latter. Men who had recently been in battle and had the classic symptoms of war neurosis or combat fatigue paid less attention to their filarial symptoms than those who had been psychoneurotic before they became infected.

The following conclusions were reached the disease soon dies out after removal of the patient from the endemic area rehabilitation is best obtained by a combined programme of military vocational, educational and medical training and supervision no impairment of sexual function has resulted from filariasis and severe sequelae have occurred in only 0.2 per cent. of cases in another year or so there should be no filariasis problem in the U.S.A.

J F Corson

SAPHIR, W. Filariasis. Early Clinical Manifestations. An Analysis of Thirty-Five Cases. *J Amer Med Ass* 1945 Aug 18 v 128 No 18 1142-4

The author studied 35 patients whose history and symptoms suggested that they were suffering from filariasis although no microfilariae were found in the blood.

The commonest early symptom was a feeling of numbness or weakness in an arm or leg which was apt to fall asleep especially at night. Soon afterwards aching developed in one or more limbs, particularly after doing heavy work this usually began in the axilla or groin and led the patient to discover his large and tender lymph glands in those parts. Later still the patient experienced periodically recurring pain in the axilla, arm, groin, thigh or scrotum, sometimes accompanied by swelling. These attacks lasted for varying periods, from a few hours to some days and were followed by intervals of a few days or weeks with freedom from symptoms during the day though nocturnal pain, especially in the testicle was often present. Finally the lymphatic glands became continuously palpable, though the degree of enlargement varied. This was the usual history during a month or two before admission to hospital no history of any feeling of general illness was given.

The axillary inguinal and femoral lymphatic glands on both sides were enlarged and tender in all the patients and other lymphatic glands were also affected in some patients. Centrifugal lymphangitis was not seen. Left-sided funiculitis occurred in 21 cases and in six of these there was also left-sided varicocele right-sided funiculitis was present in five. Ten had varicocele.

Lymph glands were excised in four cases they showed hyperplasia but no filariae. Eosinophilia (5-10 per cent.) was present in nine patients and these had no intestinal worms.

The author thinks that the symptoms observed permitted a presumptive diagnosis of filariasis to be made.

J F Corson

CULBERTSON J T ROSE H M & OLIVER-GONZALEZ J. Chemotherapy of Human Filariasis by the Administration of Neostibosan. *Amer J Trop Med.* 1945 May v 25 No. 3 271-4

Thirty patients were treated with neostibosan in Porto Rico. Five were adult males and twenty-five were girls between 8 and 17 years old. All had

microfilariae in the blood at night and all but one were free from clinical symptoms. The total dosage of neostibosan ranged from 4.6 to 10.5 gm given intravenously, in doses of 50 to 300 mgm (on alternate days for three injections and then six times a week) spread over 33-48 days. This dosage was well tolerated. At the end of treatment only two patients (whose night blood initially contained 3 and 9 microfilariae respectively per 60 cmm. blood) were free from these parasites. During the next six months however the microfilarial count declined steadily in most of the patients. After six months seven patients had become negative eight others showed a decrease in the number of microfilariae by at least 80 per cent. and in only one patient did no decline occur. Fifteen untreated young males were observed as controls. During the six months only one of these showed a decrease in the microfilarial count. [Although these results are of great scientific promise they do not justify the treatment of filarial patients with neostibosan as a practical therapeutic measure at present.]

I. Hawking

LAWTON A. H. BRADY F. J. NESS A. T. & HASKINS W. T. Tests of Mercury and Antimony Compounds in *Dirofilaria immitis* and *Latamosoides carinii* Infections. *Amer J Trop Med* 1945 May, 25 No 3 263-9 1 fig.

Tests were carried out on dogs infected with *D. immitis* and on cotton rats infected with *L. carinii*. Mercury cyanide and mercury oxycyanide had no apparent antifilarial action in dogs even when given in toxic doses. Antimony compounds of various types were given to dogs in various dose schedules. The one which was most satisfactory as regards therapeutic action and freedom from toxic effects was 0.8 mgm of antimony per kgm body weight given intravenously each day. Presumably a certain threshold level of antimony must be maintained in the blood to kill the microfilariae. Of the different antimony compounds tried sodium antimonyl 4-tertiary butyl catechol sodium antimonyl d arabitol and p-phenetidine antimonyl tartrate were the most active the blood being freed from microfilariae after 4-5 injections. However live adult worms usually persisted for many weeks afterwards the females usually showed degenerative changes in the uteri. Altogether 29 dogs were used in these experiments and 28 were freed from microfilariae by means of antimony compounds.

A small number of cotton rats infected with *L. carinii* were treated by intramuscular or intraperitoneal injections of antimony compounds. Cotton rats tolerate larger doses than dogs. The response to treatment was less rapid or complete. In rats treated with five compounds the adult worms were killed, but 10 per cent. of the microfilariae persisted in the blood until the rats were killed two months later. Four other compounds, which had proved effective against *D. immitis* in dogs were ineffective against *L. carinii* in rats. The acute toxicity of the compounds was tested by intraperitoneal injection into mice. The compound which had the most favourable ratio between therapeutic activity and toxicity was sodium antimonyl 4-tertiary butyl catechol.

I. Hawking

RIDLEY H. Ocular Onchocerciasis, including an Investigation in the Gold Coast. *Brit J Ophthalm* (Monograph Suppl V) 1945 58 pp 27 figs. & 4 pls (3 coloured) [156 refs.]

This monograph has been written by an ophthalmic surgeon who has recently served with the forces in West Africa. He there availed himself of an opportunity to investigate the eye lesions resultant on *Onchocerca volvulus* infestation of man in an area where these are known to occur. The author regards ocular

*onchocerciasis* as more terrible in its effects than the far more widespread trachoma. He deplors the lack of appreciation of its importance as a source of blindness throughout the major portion of the British Colonial Empire. It has been shown that filarial blinding is prevalent in certain limited areas of the Belgian Congo though the parasite is found extensively in this territory. In West Africa it is equally prevalent but, until very recently it has not been recognized to what extent blindness is here attributable to it. The tendency up to now has been to regard onchocercal blinding as an extreme rarity in West Africa, a view which Radley does not share.

After briefly outlining the historical aspect of onchocerciasis and delimiting its geographical distribution, the author gives an account of the morphology, life-cycle and mode of transmission of *O. volvulus*. He mentions the various anatomical sites in man from which the adults and the microfilarial forms have been recovered. The view is expressed that effective intermediate hosts other than *Simulium* spp. may exist (though no evidence is given for this belief) and the author is concerned about the possibility of extension of the range of the parasite beyond its present geographical confines as a result of troop movements into and out of the various endemic areas.

The clinical manifestations of the disease and its diagnosis are covered and the author goes with considerable detail into the eye changes he encountered in over 300 natives examined for onchocerciasis at Fumasi in the Northern territory of the Gold Coast. Of these cases, 18f had onchocercal nodules and five others were found to be suffering from ocular onchocerciasis but had no discoverable nodules. Of these 136 cases of onchocerciasis among the 300 persons examined for the disease, 51 had ocular manifestations. Visual defect ranged from blindness or near-blindness in 22 persons through varying degrees of visual defect to good sight in 29 of the 51. The author points out that the proportion of eye defects in his series may be misleading as he saw possibly a selected portion of the population in view of the known aims of his visit.

The examinations were made under difficulties in the bush but a microscope and some ophthalmic equipment, including a slit lamp were available. To the author's regret he was not permitted, owing to native prejudice to excise a blinded eye for subsequent thorough pathological examination. His detailed account of the ocular pathology of onchocerciasis is therefore largely based on the literature. But, from this and from his own slit lamp observations he states that there is now no doubt that all onchocercal ocular lesions are caused by toxins released locally by dead microfilariae and that the living microfilariae set up no tissue reaction.

The author's observations on his 51 Fumasi cases are recorded in tabular form, and fuller clinical and pathological details are given of the 22 cases with gross visual impairment. In addition to the cases at Fumasi, the author found 16 African soldiers and four African civilians in Accra to be suffering from ocular onchocerciasis. Some of these men came from reputedly non-endemic areas. In describing the differential diagnosis of onchocerciasis the suggestion is made that the keratitis, iritis and choroïdo-retinitis attributed to trypanosomiasis may in fact be due to a concurrent onchocerciasis and not to the trypanosomal infection. Radley states that personal examination revealed no ocular complications other than mild papilloedema in just over 100 cases of trypanosomiasis in the absence of an onchocercal infection.

The opinion is expressed that there is no effective treatment of onchocerciasis and that even removal of the nodules is of limited value as the individual microfilariae can survive for long periods (in one quoted case for at least 8 months) after excision of all known nodules. The author points out the difficulties in the prevention of the disease and concludes by reiterating

its gravity. There is a comprehensive bibliography appended and there are good microphotographs and photographs in the text. A. R. D. Adams

GETZ L. Massive Infection with *Trichuris trichiura* in Children. Report of Four Cases, with Autopsy. *Amer J Dis Children* 1945 July, v 70 No 1 19-24 1 fig [Refs. in footnotes]

Routine examination of stools reveals a high incidence of *Trichuris trichiura* in Panama (presumably in children especially). Exact statistics are however not available. The author quotes the study of 160 cases of infection of children with multiple intestinal parasites by EINHORN MILLER and WHITTIER (this *Bulletin* 1945 v 42 911) and a clinical survey of trichuriasis in children to be published in the same journal by the same authors.

Getz analysed 1,307 autopsies which he did between 1924 and 1929. Among these subjects 374 (28.6 per cent.) harboured worms and among these 374 *Trichuris* occurred either alone or together with other intestinal parasites in 100 (7.6 per cent.). The maximum number of parasites found in any one subject was 400 and the heaviest infestations occurred in children. The author gives a valuable survey of the literature about trichuriasis and concludes that *Trichuris* may cause serious symptoms and physical signs, especially when infestations with it are massive as they may be in young children in Panama. The four subjects described in this paper support this view.

The first subject was a mestizo girl aged 13 years weighing only 52 lb. She had been passing four to eight watery stools daily. The parents had not detected blood in them. She had suffered from weakness and loss of weight for three months. She was acutely ill and emaciated, with a temperature of 101.4°F. There was a marked pallor of the mucosa of the lips; the conjunctiva was bitish white and the palms and soles were waxy yellow. The heart, liver and spleen were enlarged. Examination of the blood revealed a haemoglobin value of 30 per cent. (Sahli), 2,300,000 erythrocytes per cmm and 3 per cent of eosinophils but no malaria. Examination of the stools revealed *Entamoeba histolytica* and eggs of *Trichuris trichiura*, *Ascaris lumbricoides* hookworm and larvae of *Strongyloides stercoralis*. The patient was treated with emetine hydrochloride for three successive days and then with oil of chenopodium but died on the fifth day. Autopsy confirmed the points mentioned above. In the small intestine there were a few *Trichuris* and six *uncinarias*. From the caecum downwards throughout the whole large intestine and including the appendix there were more than 1,100 specimens of *Trichuris* and a number of others were lost. The mucosa of the large intestine and caecum was injected and covered with mucus in which *E. histolytica* was found. There was dilatation of the heart, pulmonary oedema, fatty liver and secondary anaemia.

The second subject was a mestizo boy aged four years weighing 24 lb. He had had bloody diarrhoea, fever and cough for three days. He also was acutely ill showing signs and symptoms essentially similar to those shown by the first subject. The rectal mucosa was prolapsed and several specimens of *Trichuris* were seen moving about on the prolapsed tissue. This is not uncommon in Panama children. Examination of the blood of this subject revealed a haemoglobin value of 30 per cent. (Sahli), 2,300,000 erythrocytes per cmm and 4 per cent of eosinophils but no malaria parasites. In the stools the eggs of *T. trichiura* and *Ascaris lumbricoides* were found. The boy died 23 hours after admission to hospital. Autopsy revealed near the ileo-caecal valve one *A. lumbricoides* and a number of *T. trichiura*. In the caecum and ascending colon there were eight masses of *T. trichiura* numbering more than 1,700 altogether. No amoebae were found. There were small ulcers in the lower sigmoid and rectum. There was dilatation of the heart, enteritis, colitis, secondary anaemia and emaciation.



The third subject was a mestizo girl aged 7 years, weighing 24 lb. She had had diarrhoea for six weeks, with fever and swelling of the face for five days. She was emaciated and could not stand. She showed the same external evidences of secondary anaemia as the two previous subjects, and in addition oedema of the face, hands, abdomen and lower extremities. Examination of the blood revealed a haemoglobin value of 30 per cent. (Sahli) 2 400 000 erythrocytes per cmm. 3 per cent. of eosinophils, but no malaria parasites. The Kahn and tuberculin tests were negative. The stools contained eggs of *T trichiura* *Necator americanus* *Ascaris lumbricoides* but no *Entamoeba histolytica*. Blood transfusions and a course of hexylresorcinol failed to prevent her death 19 days after admission to hospital. Autopsy revealed 140 'unclimaries' in the small intestine between the caecum and the anus 4 100 *T trichiura* were counted. Some of these were in six or eight masses they also occurred in the appendix. There was secondary anaemia, acute cardiac dilatation pulmonary oedema and fatty changes in the liver and myocardium.

The fourth subject was a mestizo girl, aged 7 years weighing 40 lb. She had had shortness of breath swelling of the face and hands and dark red urine. She was emaciated and sunk in deep coma with a temperature of 101°F. She had oedema of the face, hands, abdomen and lower extremities. Examination of the blood revealed a haemoglobin value of 30 per cent. (Sahli) 2,300 000 erythrocytes per cmm. 4 per cent. of eosinophils but no malaria parasites. The Kahn test was negative. The stools contained eggs of *T trichiura* but no *E histolytica*. The patient died in 30 hours. Autopsy revealed that the primary cause of death was acute haemorrhagic nephritis. It also revealed pericardial effusion a dilated heart and about 250 cc. of fluid in the peritoneal cavity. In the large intestine more than 400 specimens of *T trichiura* were counted, but there was no ulceration. Like the other three she had secondary anaemia. The author concluded that although the first patient harboured five species of parasite, the infestation with *Strongyloides* and *Ascaris* were mild, because they were not found at autopsy after five days in hospital. The *Necator* infestation in this patient was also probably mild. *E histolytica* may have been important but the *Trichiura* infestation was the predominant feature. In the third the *Necator* infestation may have been a contributory cause of death. In the second the *Ascaris* infestation was not significant. In the fourth the haemorrhagic nephritis was the primary cause of death, but this subject was the only one of the four who harboured *Trichiura* only and this must have debilitated the child. The first three illustrate well the view expressed by CRAIG and FAUST (*Clinical Parasitology* 3rd edn. 1943 p. 241) that clinically heavy infestations with *Trichiura* may suggest severe hookworm disease. The most important signs of severe *Trichiura* infestation are diarrhoea, blood-streaked stools, weakness and loss of weight, with pallor, fever, emaciation, anaemia and abdominal distension. The autopsies showed that the *Trichurids* may invade the whole length of the large intestine but that there may be no characteristic lesions. Gets has examined subjects with the proctoscope and has found that the whole wall of the lower part of the descending colon and of the sigmoid may be covered with an almost continuous film of living moving trichurids. Infestation with *Trichiura* is however usually considered to produce only mild clinical effects (the author refers, for example to FERNÁN NÚÑEZ this *Bulletin* 1927 v 24 1002). These four subjects show that its effects can be severe, and in his survey of the literature, the author refers to other instances. It seems certain that the prolonged diarrhoea and anaemia may result in cardiac failure and death, but we still do not know how *Trichiura* causes anaemia.

G. Lafage

## DEFICIENCY DISEASES

GILLMAN T & GILLMAN J Powdered Stomach in Treatment of Fatty Liver and other Manifestations of Infantile Pellagra Its Significance with reference to the Problems of Edema and Steatorrhea in Infants and in Adults. *Arch Intern Med* 1945 Aug v 76 No 2 63-74 [Refs in footnotes]

In this paper the authors amplify their views as to the aetiology and pathology of infantile pellagra in Africans seen in Johannesburg and record the continuing success of treatment with a preparation of powdered stomach. In previous papers [this *Bulletin* 1944 v 41 1057 1945 v 42 748] they reported rapid cure in each of six cases treated in this way together with administration of a good diet they now record three more patients in whom the same satisfactory result was achieved and they again mention the cases previously treated with vitamins or with liver preparations in whom the results were poor most of the patients dying. The chief clinical findings in these children were dermatitis (sometimes with exfoliation and ulceration) a smooth atrophic tongue cheilosis oedema of various degrees enlargement of the liver (due to accumulation of fat in the liver cells) microcytic anaemia reduction in serum protein especially albumin (but the oedema is not related to this) and the passage of bulky offensive stools containing a high proportion of fat.

As a result of their observations the authors conclude that the liver kidney and stomach are closely interrelated in the control of water metabolism one of the striking features of treatment with powdered stomach was the dramatic disappearance of the oedema. Another effect was the disappearance of the steatorrhea. The cause of steatorrhea in coeliac disease and sprue is not well understood but the suggestion is made that in infantile pellagra there is first a dietary deficiency and vitamin imbalance which leads to disturbance of fat metabolism that the continuous presence of fat in the alimentary tract leads to the formation of enterogastrone a hormone which inhibits gastric activity by suppression of the formation either of the intrinsic factor or of hydrochloric acid. Prolonged inhibition as in chronic sprue may eventually result in complete suppression of all the functional activities of the stomach. The thesis is advanced that though in the first place the dietary deficiency is responsible for initiating the changes of infantile pellagra they lead to secondary changes and that where these occur treatment by administration of vitamins is no longer capable of restoring the normal condition. Treatment with dried stomach corrects these secondary effects. A disease at a certain stage loses its connection with the initial cause. The subsequent course of the disease may then be determined by the secondary pathologic changes.

The dose of powdered stomach was 10 gm daily for five days.

[These findings are evidently of great importance in saving life. It may perhaps be permissible to emphasize the fact that this syndrome which reflects the bad state of nourishment of these unfortunate people is preventable by action to ensure an adequate diet.]

Charles Wilcocks

MEYERSBURG H A. Senile Psychosis and Pellagra. A Report of Two Cases. *New England J of Med* 1945 Aug 9 v 233 No 6 173-6 [28 refs.]

Senile psychosis may be simulated by pellagrous encephalopathy in the aged. The underlying neurologic alterations in the elderly patient may predispose to this occurrence.

The senile-pellagrous type of encephalopathy may respond well to treatment with crystalline vitamin B products or with natural vitamin B concentrates. The recognition of this group of cases may permit effective therapy.

The maintenance of an optimal dietary by the normal aged person as well as by the senile invalid should be a matter of primary importance."

SPIES T D PERRY D J., COGSWELL, R. C & FROMMEYER, W B Ocular Disturbances in Riboflavin Deficiency *J Lab & Clin Med* 1945 Sept., v 30 No 9 751-65 6 figs. & 4 coloured figs. on 1 pl. [20 refs.]

From among patients attending the Nutrition Clinic of the Hillman Hospital, 500 were arbitrarily selected for treatment of these, 300 treated by at least one intravenous injection of riboflavin form the subject of this article. They were all persons who had developed ocular disease after subsisting on diets judged to be deficient in riboflavin were aged between 8 and 92 years, male and female, both white and negro. The majority were selected as having no organic disease no clinical evidence of co-existing deficiency disease and no known disease of the alimentary tract.

The subjects were for the most part treated as out patients and were observed before during and after treatment. In many cases slit lamp examinations were made bacteriological investigations were carried out in 50 cases riboflavin blood levels determined in 50 and urinary levels in 50 by the microbiological method. Dietary studies were made from data supplied by the patients and these in general, suggested a 64 per cent deficiency of riboflavin intake. The common complaints were nervousness insomnia, headache burning and aching of the legs and feet, burning and cramping of the stomach, constipation burning of the skin itching and burning of the eyes and falling vision, symptoms which waxed and waned in intensity 154 had cheilosis [angular stomatitis] at some time on one side only in 13 but none had the abnormal redness of the lips [cheilosis] in 2 the tongue was magenta red in 12 the naso-labial folds were affected.

Conjunctivitis both bulbar and palpebral, was sometimes the sole manifestation. In all 300 "it was observed that small vessels encroached on the cornea at the scleral corneal junction [not further defined] Circumcorneal injection was grossly visible in 80 per cent. interstitial [sic] keratitis was present in 60 per cent. and corneal ulceration in 53 per cent. pterygia was noted in 50 per cent.

The case notes of three subjects are given at length.

[This article contains nothing essentially new its chief value lies perhaps in the fact that the authors have come to recognize as others have done how great is the uncertainty concerning riboflavin and deficiency disease. They say—"We freely admit that we do not know what specific ocular symptoms and lesions are caused by riboflavin deficiency After stating that "It is only by determining the effect of riboflavin therapy on the ocular manifestations that a diagnosis of riboflavin deficiency can be made the authors add—"that this method of diagnosis and treatment is unsatisfactory we know In regard to the symptoms described, they say— It is to be admitted freely that the picture described is not one which is pathognomonic of riboflavin deficiency or one that can be immediately and specifically differentiated from superficial inflammation of the eye from numerous other causes. Again "this therapeutic test may in itself not be thoroughly valid because we have gained an impression that most inflammatory disorders of the superficial portions of the eye may be benefited to some degree by an excess of riboflavin to the organism. "All our studies on the riboflavin content of the blood tend to indicate that there is little or no fall in the concentration of riboflavin even in the presence of severe lesions." In fact, anyone about to write upon

the subject would do well to remember the authors final conclusion— we must admit at this time riboflavin deficiency is little understood. ]

H S Stannus

FERRELL Lydia. Nutritional Deficiencies in Hong Kong before the Japanese Invasion  
*Brit Med J* 1945 Oct. 6 468-70

## HAEMATOLOGY

PONDER E. The Sickling Phenomenon and its Bearing on the Problem of Red Cell Structure *J Exper Biol* 1945 Aug v 21 Nos. 3 & 4 77-83  
1 fig [30 refs.]

For the purpose of description the author calls an erythrocyte which appears normal but which under suitable conditions becomes a sickle cell a promenisococyte. In vaseline-sealed cover glass preparation the plasticity of the promenisococyte becomes increased after a period of time which varies with the thickness of the preparation the temperature and other factors. The rim of the cell becomes progressively thinner on one side until usually within one to two minutes continuity breaks down. The crescent so formed then opens out rapidly within about a second and the thin stretched concave edge expands into a series of veil like projections. At the same time the total length of the crescent contracts but the mean cell thickness increases and the volume does not change. After some hours or days the cell rounds up becomes a polytic sphere and is haemolysed. As the crescent opens up one or more slender filaments arise from each point  $10\mu$  or more in length and shorter filaments may extend outwards from the scalloped concave edge of the crescent. If the sickle cell is retransformed into the discoid form the long filaments break off at their bases and contract into rods or globules which can be seen floating freely in the plasma. Sometimes the rim of the promenisococyte thus irregularly giving rise to very bizarre forms of cell.

Oxygenation of a sickle cell results in lengthening of the crescent with increase of its curvature while at the same time the concave border extends further and becomes smoother until finally the points of the arc meet and the discoid form is re-established. At the junction of the points of the arc a small globule is formed and occasionally the filaments remain tangentially attached to the cell at this point for some time. Reversal of a sickle cell to discoid form under suitable conditions usually takes some minutes. A cell sickling for the second time does not necessarily break at the region of the previous junction.

Sickle cells undergo no sudden changes of shape on the addition of rose bengal lecithin or saponin. They remain as sickles until the time of lysis when they turn into spheres or fade from view unlike normal cells which before haemolysis become spherocytic under the action of the first two agents and crenated by the last. The ghosts of sickle cells so obtained are however never sickle-shaped but always irregularly spherical while ghosts obtained by lysing sickle cells with water are discoidal in conformity with the rule that mammalian water ghosts are biconcave discs although they often show considerable crenation. Exposure of meniscocytic ghosts to low oxygen tension does not result in any change in shape of the sickling type since the presence of haemoglobin in the cell is necessary for the transformation from discoid to sickle shape.

The shape of erythrocytes is probably determined by a balance of forces. The force of surface tension tends to produce a spherical form while it is suggested the forces which maintain the cell as a biconcave disc are repulsions

between the side chains of radially arranged cephalin molecules. To account for the sickle-cell process it is necessary to suppose that the haemoglobin in the cell exerts an "expansive force" a function of the oxygen tension. In the normal cell this force produces only tension, but in the promeucocyte, owing to some defect in the ultrastructure [presumably the molecular structure] of the envelope it produces sickling. It is suggested that the inability of the ghost cell to form spheres is due to the disappearance of the forces associated with the haemoglobin while the forces of surface tension become equal both inside and outside the ultrastructure. Leptoscopic measurements have shown the normal red cell envelope thicker by some 30 to 50 Å in the region of the biconcavity than elsewhere and that this difference is increased by organic solvents. The question now arises whether haemoglobin is distributed uniformly throughout the cell, either as a highly viscous solution or as a gel, for it becomes absent from the veil like material of the sickle cell, a material which corresponds to that of the biconcavity of the normal disk. It may be that during sickling the surfaces of the ultrastructure in the region of the biconcavity come into apposition and so drive the pigment into the body of the memocyte this explanation retains the idea that the haemoglobin is in solution. An alternative type of explanation is that the pigment is not in solution, but is combined or imbedded in a cytoplasmic matrix and that it leaves the region of the biconcavity by a process similar to that of protoplasmic streaming.

F. Mergatroyd

DRAGANOV D. V. Neurological Complications in Tropical Macrocytic Anaemia. [Memoranda.] *Brit Med J* 1945 Oct. 9 481

## DERMATOLOGY AND FUNGUS DISEASES.

FOXZARI M. Algumas causas desencadeantes do pénfigo foliáceo [Causes precipitating (the Onset of) *Pemphigus foliaceus*] *Brasil Medico* 1945 July 21 & 23, v. 59 Nos. 29/30 281-4 4 figs. English summary

Some authorities regard *Pemphigus foliaceus* as an allergic manifestation, or as the author calls it, pathergic, by which term we are to understand that some agent as it were pulls the trigger and sets the disease going. Such a precipitating agent may be a streptococcus or a mosquito-bite for example. The history of one case was as follows. A man of 23 working as a woodcutter complained of difficulty in swallowing for 10 days or so. He was then bitten by a mosquito on an eyelid. A bulla formed, followed by others in various parts of the body. Acute pemphigus ensued and death occurred five days after his admission to hospital. Another referred the onset of his attack to being bitten by ticks while he was working in a wood. This resulted first in itching and burning and later in bullous formations and pemphigus. In yet another case the origin of the disease was definitely associated by the patient with his having scalded his foot and hand with some fat some three months before. Bullae broke out burst and healed with scarring. Then other bullae appeared in other parts of his body which ulcerated and a condition of pemphigus set in and death took place soon after his admission to hospital.

The author accounts for the failure of sulphonamides and penicillin to cure—and he quotes half a dozen cases in which penicillin was administered in doses ranging from 100,000 to over a million units—by saying that, though the secondary or concomitant infection might be overcome the pemphigus continued on its way unchecked.

H. Harold Scott

BIANCHI A L Micetomas podales por actinomices y por micotorulas  
[Mycetoma of the Foot.] *Rev Asoc Med Argentina* 1945 June 30 v 59  
No 560 700-704 5 figs

A report of two cases and a discussion of the classification of fungi in relation to human disease

BUTT E M & HOFFMAN A M Healed or Arrested Pulmonary Coccidioidomycosis. Correlation of Coccidioidin Skin Tests with Autopsy Findings *Amer J Path* 1945 May v 21 No 3 485-505 12 figs on 5 pls. [10 refs.]

The correlation of the coccidioidin dermal reaction with coccidioidomycosis and calcified pulmonary nodules has been discussed by many writers and this literature is summarized in a paper by COE and SMITH (*Arch Pathology* 1939 v 27 717-34)

The present work deals with the post mortem pathological study of patients on whom the coccidioidin test had been made. The Santa Fé Coast Lines Hospital in which the study was made receives patients from a wide area which includes most of the known endemic areas of coccidioidomycosis. As the patients are members of the Hospital Association they return regularly and may be kept under observation for a long time (in some cases for 25 to 30 years) and eventually an autopsy may be obtained. Of 1165 patients tested with coccidioidin 302 (25.9 per cent) gave positive reactions. The incidence of positive reactors amongst patients from the major endemic areas was from the San Joaquin Valley 62.8 per cent, Arizona 28.0 per cent, and Texas 35.7 per cent.

Autopsy was made on 36 patients of whom 11 had been reactors to coccidioidin. Nearly all of these 11 showed pulmonary calcareous or fibrous nodules and parasitic spherules were found in the healed lesions of eight but in only five could the spherules be identified with certainty as *Coccidioides immitis*. In none of these positive reactors was a clear clinical history suggestive of coccidioidal disease obtained. Of the 25 patients negative to coccidioidin, all but four had calcified nodules in the lung but in only one of these were (very dubious) spherules found.

The calcified lesions of coccidioidomycosis are indistinguishable grossly from similar lesions of tuberculosis except that apical scars are not found in uncomplicated healed or arrested pulmonary coccidioidal disease. Inoculation of material from some of the cases into guineapigs and attempts at culture suggest that most of the lesions are mycologically and bacteriologically sterile.

As with the tuberculin test and tuberculosis there seems to be a rough quantitative relationship between the coccidioidin skin reaction and the activity or age of the primary coccidioidal lesions. The coccidioidin reaction may be negative in advanced and progressive coccidioidomycosis and it is probable that it may become negative in some patients with healed lesions. There is apparently no cross-allergic relationship of tuberculin and coccidioidin and no cross-relationship between the coccidioidin test and similar tests with the allergens of *Blastomyces Aspergillus* or *Sporotrichum* J T Duncan

MOSTO D & IARICCI V Presentación de un caso de granuloma por *Paracoccidioides brasiliensis* [Description of a Case of Granuloma caused by *Paracoccidioides brasiliensis*] *Rev Asoc. Med Argentina* 1945 July 30 v 59 No 562 826-30 11 figs.

Paracoccidioidal granuloma was formerly mistaken for the coccidioidal granuloma of Posadas-Wernicke but DE ALMEIDA in 1930 showed that the parasitic spherules of the causative fungus differed from those of *Coccidioides*

*sponds* in having no internal spores, but instead an external surrounding zone of small spore-like reproductive bodies. The fungus was therefore placed in a new genus *Paracoccidioides* Almeida 1930 as *Paracoccidioides brasiliensis* (Splendore) Almeida 1930. The disease called paracoccidioidal granuloma, is regarded as clinically more closely related to Gilchrist's disease or North American blastomycosis than to coccidioidomycosis. The authors describe four cases of paracoccidioidal granuloma in Argentina, three of which had been published previously in two of these three there was extensive involvement of the lungs, with cavitation in one case, and in both there were ulcerating granulomatous lesions in the mouth. In the third case there was extensive disease simulating carcinoma of the head of the pancreas extending to adjacent abdominal viscera. In all cases there was localized adenopathy with caseation and suppuration in some of the glands. The diagnosis was based on histological examination of tissue obtained by biopsy which showed the characteristic granuloma composed of great numbers of multinucleated giant cells and histiocytes containing the parasite (a thick walled spherical body varying in size from 1 to 30 $\mu$  surrounded by a zone of small bud-like bodies) plasma cells lymphocytes and eosinophiles. Suppuration was associated with a fibrino-leucocytic exudation which, the authors believe is provoked by a secondary bacterial invasion. In one case the diagnosis was confirmed by inoculating the sputum into the testis of a guinea pig with reproduction of the disease and in the other two by post-mortem examination. Tuberculosis was excluded in all cases. In the fourth case hitherto unpublished, the lungs were involved and there were associated granulomatous ulcerating lesions in the mouth with adenopathy of related lymphatic glands. The ulcers in the mouth were covered with a whitish exudate suggesting leucoplakia and were painful and bled on contact. The patient suffered from loss of weight and anorexia with a febrile condition increasing with the progress of the disease.

Paracoccidioidal granuloma has only recently been found in Argentina and involvement of the lungs is believed to be comparatively rare occurring in only about 15 per cent. of the cases as compared with 95 per cent. in coccidioidal granuloma.

J. T. DUNCAN

## HEAT STROKE AND ALLIED CONDITIONS

PARK, R. G. Disorders due to Heat. *New Zealand Med J* 1945 June v 44 No 241 128-31

One of the objects of this paper says the author is to pass on some practical points learnt in four years of tropical military medicine. He first discusses hyperpyrexia, when he emphasizes that the primary disorder is a failure of the sweat glands. In the dry heat of North Africa little hyperpyrexia was seen [but in the hotter Arabian desert WATERLOW HUDSON and LADELL did encounter such cases]. Hyperpyrexia must not be confused with cerebral malaria. After excessive sweating there may be a heat exhaustion there is here peripheral circulatory failure and the general picture of shock. The author outlines the nervous and humoral control of the sweat glands and the effect of drugs upon sweating. He then describes the clinical effects of hyperdrosis of which the most important is heat cramp their diagnosis and treatment. [There is some confusion in this paper between pathological hyperdrosis and the high sweat rates that occur naturally in extreme heat for the former the author recommends X-rays sympathectomy or belladonna.

Administration of water and salt is advised as treatment of the effects of excessive sweating but the importance of water and salt as a prophylactic against these effects is not emphasized.]

For prickly heat a calamine lotion is recommended. Hot climates aggravate sweaty feet but infection is equally important and the condition may be constitutional. Some relief may be obtained by avoiding heavy boots or rubber shoes. Skin hardeners such as spirit or formalin prevent maceration and infection a powder containing salicylic acid should be used after drying the feet. A cream containing hexamine which when wetted with sweat from the feet released formalin, is useful in mild cases. The relief given by X rays is usually only transient

W S S Ladell

## MISCELLANEOUS DISEASES

PAVLOVSKY E N Natural Focal Localization of Human Transmissible Diseases and the Concept of Landscape as an Epidemiological Factor *Med Parasit & Parasitic Dis* Moscow 1944 v 13 No 6 29-38. [In Russian.]

In the course of numerous parasitological surveys throughout the Soviet Union by expeditions led or organized by the author observations were made on certain peculiarities in the distribution of some transmissible diseases which are of epidemiological importance. Some of these diseases manifest a natural focal localization within well-defined geographical areas (biotopes) where the pathogenic organisms their vectors and hosts form an ecological association (biocoenosis) enabling the infection to circulate for indefinite periods of time from donor-host via vector to recipient host. One of the characteristics of such a focus of infection is its complete independence of man (and domestic animals). However human beings temporarily entering such a locality expose themselves to bites of the vector and may become infected. Furthermore if man settles down to live in a zone where such foci exist one of the following relations will be established between him and the focus (a) The focus might prevail over man giving rise to outbreaks of the disease (b) the economic activities of man might bring about the extinction of the focus or (c) the focus might continue to exist in proximity to but not in contact with man with the result that it remains potentially dangerous.

This type of focal localization has already been discovered for a number of diseases. Thus in the desert areas of Central Asia, oriental sore occurs naturally among gerbils which share their burrows with the sandfly vector. This disease is a typical zoonosis being transmissible to human beings when these come into contact with sandflies infected from the rodents which represent the reservoir host [see this *Bulletin* 1944 v 41 331]. Similarly the foci of spring-summer encephalitis are found in uninhabited forest areas of eastern Asia, where the infection is maintained in various wild animals and in the tick vector. When bitten by ticks human beings become infected the result of the infection differing according to the dose of virus received if this was large the infection develops all the symptoms of encephalitis if it was small active immunity is acquired. Focal localization also occurs in various tick-borne typhus fevers (tsutsugamushi, Rocky Mountain fever and similar diseases in the Soviet Union). One of the expeditions led by the author discovered in the steppe zone of the Krasnoyarsk territory (Siberia) natural foci of typhus fever affecting wild rodents (marmots, field mice and hamsters) and transmitted by ticks (*Dermacentor nuttalli*). Like other zoonoses this disease



is maintained independently of man who becomes infected accidentally when attacked by the vector. Among other diseases with a natural focal localization independent of the human host the author mentions plague, tick borne relapsing fever, tularaemia, Japanese encephalitis, yellow fever, brucellosis, rabies, probably kala-azar and sandfly fever and possibly also various typhus fevers (both louse- and tick borne).

The natural foci of transmissible diseases can remain undetected and dormant for indefinite periods of time as long as human beings do not come into contact with them. They therefore constitute a potential epidemiological danger and it is important that their existence should be recognized beforehand. Since such foci are characterized by definite geographical peculiarities which can serve as indicators of the presence of certain diseases in such areas a knowledge of what is termed the landscape epidemiology is useful in determining the potential danger of places about to be occupied by man. Thus the tundra zone of Siberia is the habitat of numerous blood-sucking Diptera and may harbour foci of tularaemia. The forests (taiga) of the Far East represent the endemic zone of tick-borne encephalitis while tick-borne typhus fever occurs in the region of wooded plains of Siberia. On the other hand, the desert regions of Middle Asia contain the typical biotopes of oriental sore and tick-borne relapsing fever.

C. A. Hoare

HODES, P. J. & WOOD, F. C. Eosinophilic Lung (Tropical Eosinophilia). *Amer J Med Sci* 1945 Sept. v 210 No 3 288-95 2 figs.

A helpful contribution in attempting to contrast fundamental differences between eosinophilic lung and Loeffler's syndrome. The authors give a brief sketch of the literature on the subject of eosinophilic lung and then describe two cases observed by themselves: one an Anglo-Indian from Calcutta, the other an Indian from Madras. Both had a little fever to 102° in the former to 101° F in the latter with leucocytosis 21,000 and 40,000 per cmm respectively and eosinophiles 38 and 65 per cent. soft mottled patches in the lungs and disappearance of symptoms on treatment with neosarphenamine.

The differences between this and Loeffler's syndrome are given as absence of asthmatic attacks, more developed nodules seen in X-ray pictures, less degree of leucocytosis, transiency of lung conditions, more seasonal (especially prevailing in the summer months) and occurring in temperate climates as well as in the tropics and subtropics, all being characteristics of Loeffler's syndrome.

H. Harold Scott

LEE, R. K. C. & FANG, H. Q. Ichthyotoxism—Fish Poisoning. A Report and a Review. *Amer J Trop Med* 1945 May v 25 No 3 281-5

Of the two forms of fish poisoning that by toxins present in the living fish and that inserted by wounds inflicted by the spines, the present article deals with the former. Two outbreaks occurred in Honolulu in the last two months of 1944, the persons attacked numbering 34 and 14 respectively and all showed symptoms a few hours after ingestion of sea bass, *Paralichthys louti* and *Serranus fasciatus*. The fish appeared to be quite fresh. Animals to whom some of the fish was given were also poisoned.

The symptoms in the human cases were much the same in all. They might set in within a couple of hours or be delayed for 6-7 hours. They started with diarrhoea and some abdominal pain (not severe), the stools were liquid, light in colour at first and frequent, every 10-15 minutes. An hour or two later there would ensue a numb sensation in the lips and mouth with aching of limbs, perhaps severe enough to need an opiate. At the same time there

was a burning sensation in the mouth making swallowing difficult and a feeling described as a dry ice sensation of the palms and soles 48 hours later there was itching of the hands and feet, but no rash. The patients were sufficiently recovered to be able to get about in 10 days or so but on leaving hospital the paraesthesia or itching was still present. There was no fatal case so pathological lesions could not be studied.

*Variola louti* frequents the waters of Christmas Palmyra Wake Society Fanning and Apiang Islands and near the Red Sea the *Serranus fascogut latus* much the same area. Palmyra Ponape Gilbert Marshall Christmas Tongo Reva and Fanning Islands. Both species belong to the Sea Bass or Grouper family and go by the local names of Hapapu in Hawaii Shakepan among the Chinese and Ara among the Japanese. Whether the poison arises from substances on which the fish feed or on poisons developing at the spawning season is referred to as it usually is in other papers dealing with this subject but no definite conclusion is reached. H Harold Scott

SEHEULT R. Observations on the Incidence of Cancer in Trinidad. *Caribbean Med J* 1945 v 7 Nos 2 & 3 72-84

## GENERAL PROTOZOOLOGY

JOHNSON G TRUSSELL Margaret & JAHN Frances. Isolation of *Trichomonas vaginalis* with Penicillin. *Science* 1945 Aug 3 126-8 [Refs in footnotes]

The authors have worked out a technique for obtaining bacteria free cultures of *Trichomonas vaginalis*. To 10 cc. of C.P.L.M. medium (cysteine peptone liver infusion maltose and human serum) penicillin was added to a strength of 5 000 to 10 000 units per cc. To each tube was added two platinum loopfuls of vaginal discharge known to contain the flagellate. The tubes were then incubated for 60 hours at 37°C. At the end of this period transfer into the same medium without penicillin was carried out and further transfers were made every 40 to 44 hours. Bacteria free cultures were obtained in this way from seven consecutive cases. In the early cultures the flagellates showed a tendency to grow in clumps as did the first bacteria free cultures isolated by TRUSSELL in 1939 (*J Iowa State Med Soc* 1940 v 30 66). As in his case with repeated subculture the tendency to clumping was lost.

C M Henyon

HEATH P & ZUELZER W W. Toxoplasmosis. Report of Ocular Findings in Infant Twins. *Arch Ophthalmology* 1945 Mar v 33 No 3 184-91 5 figs. [15 refs]

Identical negro twins born prematurely at the eighth month were found to have been suffering from toxoplasmosis when a post mortem examination was made of one which died at the age of one month. The other was still alive at seven months. The infection which must have occurred not later than the seventh month of gestation had caused arrested development of the eyes in which destruction of the young nerve tissue causing bilateral choroidoretinitis was detected. The post-mortem findings in the eyes of the twin that died and the ophthalmoscopic appearances of the eyes of the survivor as observed from

time to time are described in detail in the paper which is a lengthy ophthalmological report on the cases. Sera from the surviving twin and the mother both contained neutralising antibodies against toxoplasma as tested by Sabin's method.

## GENERAL ENTOMOLOGY

WIGGLESWORTH, V. B. Transpiration through the Cuticle of Insects. *J. Exper. Biol.* 1945 Aug., v 21 Nos. 3 & 4 97-114 2 pls. & 6 text figs. [42 refs.]

The paper deals with the passage of water and other substances through the cuticle of insects, and with the lipid materials which in some cases greatly reduce the water loss. The work is reviewed here in general terms to indicate the contribution which the insect physiologist is making to the understanding of some of the problems of medical entomology. It is important to us in two ways. In the first place if the insect is to live in a relatively dry environment it must reduce the loss of water through its cuticle. Its power to do so will influence its geographical and seasonal distribution and, therefore, the epidemiology of an infection which the insect transmits. But the subject is important also in a second direction in relation to the passage of the contact insecticides through the surface of the insect.

It is already known that the insect cuticle is a very complex structure. The impediment to the loss of water from the insect's body is generally ascribed to the epicuticle (which contains no chitin and is not penetrated by pore canals) more precisely the reduction of loss of water is thought to be due to certain waxy substances on or in the epicuticle.

Wigglesworth enters the subject by studying the loss of water from a number of insects which live in different habitats. He works generally with insects killed by cyanide and he finds a striking contrast in the rate of loss weighing them at intervals and he finds a striking contrast in the rate of loss of water in insects from different environments. For instance one beetle larva which normally lives in moist soil loses water at a rate approximately the same as that of an open water surface so that its cuticle offers almost no impediment to the outward passage of water. At the other end of the scale come insects with a very high resistance to desiccation and a much lower loss of water per unit area. It is also found that the rate of loss of water is a function of temperature though not directly so for in many insects there is a critical temperature above which the water loss is greatly increased. In such an insect as the cockroach this critical temperature occurs at about 30 to 35°C. so that the insect might find itself living either above or below the critical temperature. But in other insects which are more resistant to loss of water the critical temperature is above 50°C. that is, above any temperature at which the insect can live.

The loss of water from the larva and pupa of the blowfly *Calliphora* is interesting. In the larva whether it is feeding or has emigrated from the meat, the critical temperature is about 35°C. and in the young puparium it is approximately identical. But in the puparium a few days old the critical temperature is much higher and there is a much greater resistance to the loss of water. This increased resistance is not due to the thick outer skin of the puparium but to the very delicate cuticle of the pupa itself an indication of the importance of even the thinnest layer in reducing evaporation from the insect body.

Wigglesworth has also considered the effect of abrasive dusts on the wax films. It is already known that certain chemically inert mineral dusts are fatal to insects (indeed the method is used in destroying pests under certain circumstances) and that the cause of death is desiccation. In the present paper it is shown that this desiccating effect occurs only with the living insect and particularly if it moves about so as to rub some parts of its body on a surface which has been dusted. For instance the nymph of *Rhodnius* under certain atmospheric conditions loses about 2 per cent. of its weight in the twenty four hours. If it is walking on filter paper which has been covered with a mineral dust and dragging its abdomen over that surface the loss of weight may be increased ten or twenty fold depending on the nature of the dust. But if the underside of the abdomen is protected from contact with the dust the loss is only slightly greater than the normal. One may imitate this with the dead insect by rubbing parts of its body with abrasive substances. The fact that the abrasion actually removes the wax film is confirmed by dissecting off the cuticle and soaking it in ammoniated silver hydroxide. Where the wax film has been broken the underlying polyphenols are stained black, but there is no blackening where the film is intact. In this ingenious way it is shown that an abrasion occurs not only where the body drags over a surface but also at articulations and other points where body surfaces rub on one another. This is illustrated by microphotographs.

It is interesting to learn that breaches in the wax film are repaired and that this restores the impermeability to loss of water. This is associated with active changes in epidermal cells and emphasizes that insect cuticle is alive and that the control of loss of water is in no sense passive.

In a final section of the paper Wigglesworth describes experiments in which solvents and detergents are applied to the cuticle of various insects. His general conclusion is that the wax layer which overlies the epicuticle is further protected by a layer of cement. In the course of this work he was able to demonstrate that different types of detergents have different effects on the water proof layers of the cuticle and that this is reflected in the rate of entry of insecticides. For instance he secured capsules on the backs of nymphs of *Rhodnius* and in this way administered known doses of insecticides to known areas of cuticle. He found that nicotine in refined paraffin had almost no effect on the bug in two days but the same dose applied in the cetyl ether of polyethylene glycol killed all nymphs in twenty four hours.

P. A. Buxton

ALPATOV V. V. NASTUKOVA O. K. & KHARTULARI 'E. M. [Eggs of the Head and Body Forms of *Pediculus humanus* L. and their Variation associated with Conditions of Rearing.] *Zoologicheskii Zhurnal* Moscow 1945 v 24 No 1 42-7 [In Russian.]

The exact status of the head and body forms of human lice (*Pediculus*) is not quite clear. Some workers have believed them to be separate species and others that they are merely modifications of a single species. A third opinion is that there is insufficient evidence to decide. An attempt to provide this evidence has been made by a biometric study of the eggs of the two forms.

CHOLODKOWSKY (*Zool. Anz.* Leipzig 1904 v 28 368-70 and *Vo. med. Zh.* 1916 Nov-Dec.) first pointed out differences in the eggs of the two forms. TONKOVA however found differences as great between populations of each sort taken from different sources (*Izv. Akad. Nauk S.S.S.R. [Bull. Acad. Sci. U.R.S.S.]* 1927 v 21 397-404). The present authors measured six dimensions of the louse egg and took the position of the egg-cement as a seventh character. On the basis of these measurements mean figures with standard errors are given

in tabular form from which it seems quite clear that the eggs of head and body forms are recognizably distinct (judged by averages) in natural populations.

Body lice and head lice from natural sources were reared in boxes worn close to the human body and fed thrice daily on the skin of the arm. It was found that the eggs of body lice remained unchanged, but that the head lice strain laid eggs identical with the body form within five generations. Even the first generation eggs were very greatly modified towards the body type. Similar results were obtained with lice kept in a thermostat at 30°C. No explanation can be offered for the change—it may be due to selection or by inheritance of acquired characters. Temperature is suggested as the factor which may be responsible.

The significance of the possible change of head to body lice is obvious when it is considered how much more common the head form is, being relatively common even among cultured people. If conditions of hygiene deteriorated the head lice might set up a general body louse infestation, which would pave the way for a typhus epidemic.

J. R. BURRINE

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

WEST INDIES. West India Royal Commission Report. [LORD MOYNE, STUBBS R. E., CROWDY Rachel E., CITRINE, W. MACKINNON P. G. BLACKLOCK, MARY G., EAGLEDOW F. L. & HENDERSON H. D.] Cmd. 6807 pp. xviii+480 1 folding map & 16 pls. 1945. June. London H.M. Stationery Office [7s. 6d.]

— West India Royal Commission 1938-39 Statement of Action taken on the Recommendations. Cmd. 6856 108 pp. 1945 June. London H.M. Stationery Office. [2s.]

— Development and Welfare in the West Indies, 1943-44. [STOCKDALE, Frank, K.C.M.G., C.B.E. (Comptroller for Development and Welfare in the West Indies). Colonial No. 189 pp. iv+115 1945 London H.M. Stationery Office. [2s.]

This report (Cmd. 6807) makes gloomy reading. It gives an account of the West Indies from the time when slavery was established, through the period of emancipation and the 19th century when the economic situation was grossly affected by the changes in world demand for the produce of the islands, to the position which existed immediately before the war. This position was bad, as was acknowledged by most of those competent to judge. Economically the islands were poor—their produce did not bring in revenue sufficient to maintain the people at a satisfactory level of subsistence—there was growing competition abroad—the islanders largely of African origin, had lost their old tribal organizations and standards, and these had not been replaced by any new cohesive structure of society which would tend to satisfactory community life or individual dignity. The people relied for subsistence chiefly on the sale of their labour and this was wanted at the cheapest rates and was needed, under the régime of 19th century economics, only in accordance with the fluctuations of general prosperity. Part time labour of the cheapest kind was the general rule existence being supported by the small holdings which a number of the people cultivated. The result was poverty, disease and waste of natural resources by inefficient farming set in a background of ignorance and superstition. Yet the population has not ceased to increase with consequent intensification of economic stress.

The diseases prevalent in these populations are those which would be expected in such circumstances. Malnutrition is general bowel diseases helminthiasis malaria, tuberculosis leprosy yaws and venereal diseases are the great problems. The arrangements for dealing with epidemics are fairly satisfactory and no doubt the protection afforded in this matter has prevented a heavier disease incidence and mortality than has actually been experienced. Expenditure on medical services during three years before the war varied from 8.9 to 19.6 per cent. of the total expenditure of the different countries and islands the average proportion spent on medical services therefore has been reasonably in line with the proportions so spent in other countries. But the Commission comment unfavourably on the general tendency to spend too small a proportion on preventive measures and too great a proportion (but not of course too great an actual amount) on the curative services. They argue that since most of the ill-health of these Colonies is due to preventable disease a greater proportion of medical effort should be devoted to prevention with its possibility of long term benefit than has so far been the case. They admit however the difficulty a Director of Medical Services must have in diverting part of his limited funds from the improvement of the curative services since pressure of public opinion is usually directed to means for the care of the sick and the curative services themselves badly need extension. "The Commission also comment that the reason why preventive measures are not more cultivated is partly that the education and experience of members of the medical staff have been directed chiefly to curative work and that some of them lack the preventive outlook and partly that there is opposition by vested interests such as the owners of house property to needed preventive measures. The Commission condemn the view sometimes expressed, that it is useless to provide the people with good houses because they would convert the best of dwellings to the kind of slums they now inhabit [To the reviewer this ignorant and thoughtless opinion (which usually is no more than a crude rationalization) is a social evil. The extreme examples of the concentration camps of Germany indicate that if men are treated like animals they tend to act like animals. The reverse that good environment tends to produce desirable persons is the basis of all social and educational work.]"

Compared with some tropical countries the West Indies are fairly well supplied with Government doctors and with beds in Government hospitals but the needs are not by any means fully met so that more staff and more hospitals and other curative services are still demanded. There are many private practitioners but their position is not easy.

The Commission made certain recommendations for the appointment of a Medical Adviser for the whole area for the unification of the medical services for the centralization of the medical institutions for the creation of a school of hygiene for the development of long term health policies for the reorganization of the medical services and for an increase in certain preventive measures. Action was taken on these recommendations and on the general recommendations relating to other than medical matters the details may be found in the Statement of Action Taken (Cmd. 6656) which was presented to Parliament in June 1945. The Report of Sir Frank Stockdale (Colonial No. 189) also describes the improvements which have been effected during 1943-44 even under the difficult conditions of war time.

To the reviewer it seems that hitherto the dominating force which has controlled the welfare of these people has been the commercial attitude. When trade was good they were comfortable and when it was bad they were almost destitute but all the time trade was the deciding factor and all the time the people were ignorant. The medical view of life is different. Medicine is concerned with human welfare not because men are units of production but

because they are human beings having the right to good health. It is no longer a principle of British government that colonies should be developed solely for the benefit of Britain or of big commercial interests, and the principle has been accepted that Native welfare is paramount. Thus being so and good health both physical and mental, being so cardinal a factor in human welfare, it seems evident that in the future the medical services should be given much greater prominence than ever before in the formulation of general political and industrial policies, and that the criterion which should determine action should be the needs of the people rather than their immediate capacity to produce. It is not, of course, denied that the capacity to produce is important, but medicine argues that one of the vital factors in efficient production is good health and that the rest depends, within the limits of what is possible in the countries concerned, upon organization and education.

There are indications in these reports that the importance of Native welfare is seriously accepted as the leading principle of government.

*Charles Wilcocks*

**WEST INDIES.** West India Royal Commission. Report on Agriculture, Fisheries, Forestry and Veterinary Matters [ENGLEDOW F. L. C.B.G. (Drapers Professor of Agriculture, Cambridge University)] Cmd. 6608. pp viii+235 1945 June. London H.M. Stationery Office. [3s. 6d.]

This Report, which surveys the agricultural resources and needs of the West Indian Colonies, and discusses local problems of livestock and fishery developments is supplementary to that of the West Indian Royal Commission (see above Cmd. 6607) of which Professor F. L. Engledow was a member.

**INDIA.** Annual Report of the Public Health Commissioner with the Government of India for 1941 and 1942 [COTTELL, E.] 63 pp 1 folding map 1944 Delhi Manager of Publications. [Annas 12 or 1s.]

Owing to war conditions this Report though it deals with two years of work, is less than half the size of the former annual reports. The mass of statistical matter that has been excluded will be published later.

Deaths from the diseases for which reasonably accurate statistics are available were —

	1941	1942	Average for 1936-1940
Cholera	228 141	219 496	135 723
Smallpox	59,307	27 137	64,088
Plague	11 984	10,577	20,923

Figures for deaths from malaria cannot be given, they form an unknown part of the total number of deaths from fevers of every kind, and diseases other than fevers are often included under this heading. The only areas in which malaria was exceptionally prevalent were the Punjab, Delhi Province and the North West Frontier Province in which epidemic conditions occurred in 1942. The epidemic in the Punjab followed a period of heavy rainfall in July and August so that the Annual Forecast was able to give timely warning, as a result of which arrangements were made in advance for dealing with the epidemic. The attendances at dispensaries in the Punjab during the year were more than two million. In normal years they were less than one million. The deaths from "fevers" in the province rose from 528,633 in 1941 to 654,295 in 1942, and presumably the increase was due to malaria.

The number of births in India in 1941 was 9 425 671 the deaths were almost exactly three million fewer the per mille figures were 32.1 and 21.8 respectively. In 1942 the births fell to 8 714,555 and the deaths to 6,336,313 the per-mille figures were 29.4 and 21.3. As the birth rate in India had remained steady at about 34 per mille for a number of years the progressive fall since 1930 is regarded as of particular interest in view of the world-wide discussions on what is regarded as the increasing population pressure in India and the alleged failure of food supplies to keep pace with it. [This remark seems to indicate that the author did not take a pessimistic view of the food situation but it would seem desirable to make a close investigation into the alleged failure because the allegation has been made by highly responsible persons, including a Member of the Viceroy's Executive Council. The Central Advisory Board of Health which held its fourth meeting in Calcutta in January 1942 did not discuss this problem and apart from one or two brief references to research on nutrition the report makes no reference to the subject of food shortage as a public health question. This omission is not really surprising because the prevention of disease caused by inadequate diet is usually regarded as being outside the scope of public health organizations.]

Inoculation against cholera has made rapid strides in recent years. In 1941 about 13 million persons were inoculated in the provinces of India, including nearly 3½ million in Bengal. In 1942 4½ million inoculations were carried out in Madras and more than 3½ million in Bengal.

Inoculation against plague was on a smaller scale. 600 000 persons were inoculated in 1941 mostly in Bombay Madras and the United Provinces. In 1942 the inoculations numbered less than 350 000 the reduction was chiefly in Bombay where less than 20 000 inoculations were carried out against 332,437 in 1941.

The incidence of enteric fevers in India is a matter of speculation even in the few areas in which the disease is a registrable cause of death the official figures give no indication of the real prevalence of the disease. [There is reason to believe that infection is so widespread that attacks in infancy and childhood confer a considerable degree of immunity on the adult population hence the absence of epidemics on a large scale.]

The tuberculosis situation is also somewhat obscure surveys were carried out in a number of localities and the Tuberculosis Association of India has continued to do active work in organizing research relief and teaching work in connexion with the disease. A model Tuberculosis Clinic was opened in New Delhi in 1941.

It is estimated that there are about one million lepers in India. Valuable work is being carried on by the India Council of the British Empire Leprosy Relief Association and by the Mission to Lepers which cares for 10 000 in 47 homes and hospitals and for 1 000 healthy children of lepers who are segregated from their parents. The total indoor accommodation for lepers in India is 13 676 beds.

The defects of the system of registration of causes of death are exemplified by the figures for kala azar in 1941. The deaths registered in Bengal were 18,349 in Bihar 91 and in Assam 40 whereas the cases treated in medical institutions were 105 018 in Bengal 119 465 in Bihar and 16 470 in Assam. It is suggested that the deaths from the disease in Bihar are probably registered under other causes.

The announcement by SWAMINATH SHORIT and ANDERSON in June 1942 [this *Bulletin* 1943 v 40 227] that kala azar had been transmitted to every one of six [five] volunteers by the bite of *Phlebotomus argentipes* is rightly described as a most important piece of work.



A brief account is given of the health activities of the Central and Provincial Public Health Departments. Five Health Units were operating in rural areas, each of which has a population of about 40 000 and the cost of each is about 30 000 rupees yearly. These units serve as demonstrations of the value of public-health services and as places of training for workers. The birth rates in two of them are stated in one it averaged 47.7 and in the other 48.9.

Famine conditions persisted in the Hissar District of the Punjab in 1941. Germinated gram was distributed to about 140 000 persons and although the amount was only a little over two ounces twice weekly a striking improvement in health is said to have resulted. In 1942 famine relief camps had to be opened in one district in Madras. During the two years measures for the relief of famine and scarcity were needed on a very small scale.

The provincial reports on health activities show that the war caused comparatively little interference. The report from Bengal contains no hint of premonition of the disastrous famine of 1943.

Maternity and child-welfare work obviously makes a special appeal to Indians. In Madras the expenditure on this by local bodies excluding Madras City was 560 000 rupees about four times as much as in 1932. No less than four voluntary organizations in Bombay were carrying out a co-ordinated effort directed chiefly to child welfare.

The subject of medical research is dealt with in separate reports, but it is stated that the most serious curtailment due to the war was in malaria research. High hopes are entertained that the destruction of adult mosquitoes by spraying will make widespread control practicable.

In addition to the voluntary bodies already mentioned, the Indian Red Cross and the St. John Ambulance Association continued their peace-time activities though most of their efforts were naturally directed to war work.

The Tuberculosis Association of India has opened a model Sanatorium at Kasauli and has considerably expanded its work of relief, propaganda, and the special training of medical men.

The Indian branch of the Ross Institute of Tropical Hygiene continued its valuable work of supplying expert advice and help to tea plantations and other industrial concerns.

[The production of this report in war time by the contemptibly small staff of the Public Health Commissioner's Office reflects great credit on Lt.-Col. COTTER and his assistants.]

It is to be hoped that when Sir Joseph BHOZE has completed his comprehensive report on health conditions in India the governments and peoples of that country will realize the urgent need for planning and carrying out a campaign directed against all the causes of preventable disease. Hitherto the basic preventable disease malnutrition due to inadequate diet, has been practically excluded from the activities of public health departments except as a subject of research.

JOHN W. D. MCGEE

YACOB M. & SWAROOP S. Longevity and Old Age in the Punjab. [Abridged.] *Brit Med J* 1945 Sept. 29 433-6, 3 charts.

The authors discuss certain aspects of longevity in the Punjab and conclude that "the study indicates that one of the urgent needs is the making of reproduction an easy and risk free process."

The following statistics are of interest. In 1931 the expectation of life at birth in the Punjab was 28.05 years for males and 26.57 for females. For the whole of India the corresponding figures were 26.91 and 26.56.

During the five years 1935-39 the average infant mortality rates in the Punjab were 172 for males and 157 for females. Up to the age of 10

years the death rate among females was rather lower than among males but between the ages of 15 and 40 the deaths among females were considerably more numerous than among males—the rates were 30 for females and 24 for males

The authors comment on these figures is in England the rate of maternal mortality is as low as 2 or 3 for 1 000 births in the Punjab it is generally believed to be from eight to ten times this figure The absence of facilities for maternal relief and care coupled also perhaps with a rather unfavourable attitude towards the weaker sex in the Punjab are responsible for keeping female longevity at so low a level Female infanticide though no longer practised in the province is said to have persisted till comparatively recent times Sir James DOUGLAS is quoted as having stated in 1895 that fifty years after Lawrence denounced the murder of female infants we are still discussing the best method of putting down that inhuman practice

A graph is reproduced showing that from 1900 onwards the mortality rates among males and females have tended to decline

[No reference is made to the part played by the marriage of immature girls in causing the deplorably high rates of infant and maternal mortality in the Punjab as well as in the rest of India]

*John H D McGara.*

**WESTERN SAMOA** The Twenty-Second Report on the Administration of the Mandated Territory of Western Samoa, covering the Four Years from 1st April, 1941, to 31st March, 1945 [FRASER P Minister of Island Territories, 17 pp 1 chart 1945 Wellington New Zealand [6d]]

The medical staff consists of three European medical officers 22 Native medical practitioners one European and four Native dental officers one European dispenser one bacteriologist (of part Samoan descent) 11 European matrons or sisters 95 Native nurses and 39 others The hospital at Apia has a laboratory and X ray department In 1944 there were 3 538 admissions to hospital and 69,839 out patients and 425 major operations were performed

The principal diseases are now—filariasis parasitic diseases (especially hookworm) typhoid pneumonia septic sores pulmonary tuberculosis Cases of meningococcal meningitis and dengue were also reported in 1944 in considerable numbers Infectious jaundice (? leptospirosis) is also reported Infant mortality rates fluctuate considerably from year to year according to the reported figures it is not clear how comprehensive the reporting is but it is stated that in 1936 the heavy rate of 291.7 was due to epidemics of whooping cough and measles The rates in 1943 and 1944 were 124.4 and 75.8 respectively The total population as at March 31 1945 was 66 761 *Charles H Wilcocks*

**COOK ISLANDS.** Report of the Administration of the Government of the Cook Islands, including Niue for the Four Years ended 31st March, 1945 [FRASER P Minister of Island Territories] 16 pp 1945 Wellington New Zealand. [6d]

The medical staff consists of two European medical officers and six Native medical practitioners four European sisters and 20 Native nurses one European dental officer and two Native dental assistants In 1944–45 for the population of 14,506 the health service expenditure was £12,724 representing 17s 6d per person For the same year in patients numbered 448 and out patients 8 603 and 101 major operations were performed

During four years there have been mild epidemics of influenza chickenpox measles and dysentery the most serious diseases are tuberculosis filariasis

and leptospirosis. Figures for these are not given. Infant mortality rates vary very greatly from year to year no doubt because the births registered are not numerous.

The health conditions of Lower Cook Islands and Northern Cook Islands are similar. At Nukunono there is a European medical officer, a Native medical practitioner, a European matron and three nurses. Of the infectious diseases, yaws appears to be the most prevalent, but filariasis is also common. typhoid has occurred. Infectious jaundice (? leptospirosis) caused 78 cases in 1944.

Charles Wilcocks

DEUTSCHMAN Z. Public Health and Medical Services in the Philippines.

Reprinted from *Far Eastern Quarterly* 1945 Feb 148-57 [12 refs.]

This short account of the medical services of the Philippines opens with a historical survey in which full justice is done to the extensive work carried out by the United States authorities until the inauguration of the Commonwealth, and to the efforts of the local administration after that date. During the present century the population has increased from 7½ millions to 16 millions, and during that period protection against the common epidemic diseases of the far east has been reasonably effective. Energetic administration has produced for these islands a more comprehensive system of medical care than exists in most countries of that region.

Immediately before the war the Bureau of Health included five divisions (Administration, Epidemiology, Hospitals and Dispensaries, Sanitation, and Maternity and Child Hygiene) and employed 690 doctors, 1,143 sanitary inspectors, 835 nurses, and other officials. There were 45 hospitals and 1,063 dispensaries, and certain clinics at which 281 physicians were employed. Campaigns for immunization and for construction of latrines (Almost two million of these had been made by 1938) were in being. The total number of hospitals in 1938 was 160 providing bed accommodation at the rate of 0.76 beds per 1,000 population (U.S.A. 9.7 per 1,000). There were 4,909 licensed physicians (1 for 3,216 of the population, a very high rate for the far east) and 5,030 registered nurses. The numbers of dentists, pharmacists and midwives were also large. There are four medical schools.

With the increasingly effective control of smallpox, cholera and plague (the last of which has not occurred since 1914) the health problems are more of the sub-tropical than the tropical type and the diseases concerned are tuberculosis ("the most important cause of death"), malaria (a disease of the foot hills),

and nutritional diseases. Steps have been taken to deal with these but they are still serious problems.

Charles Wilcocks.

CORRYN E. N. The Pilgrimage to Mecca. Medical Care of Pilgrims from the Sudan. *Lancet* 1945 Oct. 6 445-6.

In this short but interesting note the author describes the medical mission which accompanied the Sudan pilgrims to Mecca in 1944. On their route from all parts of Africa the pilgrims pass through Suakin. In 1942 for the first time a Sudanese doctor himself a Moslem, accompanied the pilgrims to Mecca, and by 1944 the experience gained enabled the authorities to send a full mission consisting of two medical men, one medical assistant, one sanitary overseer and a hospital staff of seven (one a woman), one cook, one storekeeper and two ambulances with their drivers. A tented hospital of 30 beds was set up near Jedda and dispensaries at Mecca and Medina. Sudan pilgrims only were admitted as in-patients to the hospital, but out-patient treatment was given to all who desired it.

The venture was a great success and much use of these medical facilities was made by the pilgrims the total cost was about £5 000 Improved conditions in the camps at Suakin have added to the comfort of these travellers some of whom may be away from their homes elsewhere in Africa for two years before completing their journey

Charles Walcocks

TEIXEIRA Q de A Fiscalização sanitária dos aeroportos. [Sanitary Control of Airports.] *Folha Med* 1945 Apr 25 May 5 & June 5 v 26 Nos 8 9 & 11 59-64 67-72 84-8.

This article may be regarded as a summary of lectures on aerodromes aeroplanes and the health of their crews and passengers, and the measures to be taken to avoid transmission of disease by vectors insect or human These lectures form part of a course on Public Health at the Oswaldo Cruz Institute Hence there is little here which lends itself to abstract since the whole is really devoted to pointing out the necessity for the rules which have been laid down and the dangers which would follow (and indeed have followed) neglect in carrying them out Tables are given recording the insects found, dead or alive in aeroplanes coming to Miami Florida in 1939 from Mexico Trinidad, Porto Rico Colombia Venezuela and elsewhere The average incubation periods of various infectious diseases are given showing that all of them or practically all, are longer than most flights even long-distance and so stressing the importance of careful examination of crews and passengers and adherence to the regulations of the Pan American Bureau laid down in 1937 Disinfection of the aeroplane can be carried out during the flight by means of a spray containing pyrethrum and carbon tetrachloride in kerosene [DDT receives no mention] The regulations of the Argentine authorities for disinsection of aircraft (Jan. 1943) are quoted in full together with the apparatus to be carried and the details of procedure The records for 1942 for the airports of Natal and Belém are given 457 planes were disinfected, 452 at Natal 5 at Belém, 4 194 arthropods were captured, of which 4 181 were harmless of the remaining 13 the chief was *Anopheles gambiae*

As regards passengers the author favours the issue of a Sanitary Passport which gives a great deal of personal information and calls for vaccination against yellow fever smallpox and enteric fever a Wassermann test blood examination for parasites search for intestinal parasites X ray of the chest bacteriological examination of the sputum, together with the identity card, place of residence for the week preceding embarkation and any history of recent contact with suspicious cases

H Harold Scott

NAPIER, L. E. The Teaching of Tropical Medicine in the United States. *Amer J Trop Med* 1945 May v 25 No 3 233-40

The author begins by making the point that the teaching of tropical medicine as part of the general medical course for undergraduates has been neglected in the United States and in other countries During the war medical men have served in the tropics and to equip them there have been instituted short courses of admittedly insufficient scope In the next few years moreover there must inevitably be the problem of the returned service man who will need in his own home the attention of local medical men for diseases with which they are not familiar Temporary arrangements have been made for the teaching of the present generation of undergraduates but these though probably the best under existing circumstances, are not ideal

The author's suggestion is that a broader teaching in systematic parasitology and tropical diseases (including nutritional diseases) should be integrated into the general medical curriculum, and that these subjects should not be

segregated from the rest of the course. The preventable nature of most tropical diseases should commend the teaching of them to the public health instructors. In this way the "purely artificial barrier that exists today between tropical and temperate medicine" would be broken down. The study of tropical diseases would contribute much to the general understanding of medicine.

For the training of medical men who propose to practise in the tropics special schools are needed, and these should be instituted in connexion with the large medical schools preferably those in seaports. For the United States three such schools are needed at first. A comprehensive syllabus is suggested, covering a course lasting 8 or 9 months, with about 1 000 hours of instruction.

Charles Wilcocks

MITCHELL, J. P. Medical Education in Uganda. *South African Med J* 1945 July 28, v 19 No. 14 242-5

The author traces the course of medical education in Uganda from the days when the epidemic of syphilis demanded the instruction of Natives in the simpler principles of diagnosis and treatment to the present time, when the Mulago medical school educates selected Africans, through a 6-year course to a stage at which they are competent to take charge of hospital and to perform major surgical operations. The details of the story need not be recounted here, but the author's conclusions drawn from his own long experience of these Africans during their training and after qualification, are important. He has no doubt of their capacity to do well the work for which they are trained, though he admits that for some time they will need guidance and that teaching and research will continue to demand the best European officers, but he is confident that the success of Mulago indicates that the same principles can be widely extended throughout Africa.

During the war we have had many distinguished medical visitors. All have expressed surprise that the African is capable of attaining the higher intellectual levels of the European. Only those who have worked for years with them appreciate that they can. Moreover I am frequently told that we are dealing with a more highly civilized African than is found elsewhere. We used to think so ourselves but we were mistaken. East Africans, other than the Baganda, have shown that given similar opportunities they can not only keep pace with the Baganda but outstrip them. And I would emphasize that they are the same people as I have seen all the way through Africa on journey south.

Mitchell pays tribute to the enthusiasm of those who have been selected from the European medical staff to carry out this training.

Charles Wilcocks.

JOHNSON, M. S. Rodent Control on Midway Islands. *U S Nav Med Bull* 1945 Aug, v 45 No 2 384-63

The Midway Islands (Sand Island and Eastern Island) in the North Pacific Ocean, have no native mammals but mice and rats have been recently introduced and have multiplied greatly. Rats were first noticed in March 1943; they have entirely destroyed two species of birds, the Laysan rail and the Laysan finch, have nearly exterminated the canaries and have no doubt reduced the numbers of other species of the island birds. They enter stores and other buildings but live mostly out of doors and commonly in the burrows of the Brown Island petrel, known as the "small moaning bird," whose eggs and young they eat.

So far only two species of rat have become established *Rattus rattus rattus* and *R. alexandrinus* the latter being three times as numerous as the former no part of the islands is free from them but they are most numerous in bush covered ground and here most of the petrel burrows are found

The use of poisoned bait seems to be the only effective method of control Experiments with various kinds of bait and poison were made and are described in detail the poisons tried included squill Antu (3 per cent alpha naphthylthiourea) and zinc phosphide the last being the best. The aim is to cover the entire area of the islands by sections the minimal requirement being that each section should be baited for one month out of every three pans containing bait are placed about 100 feet apart (4 to the acre) and unpoisoned and poisoned bait are put in them alternately the former for 8-10 days and the latter for 3-4 days The bait consists of maize meal 14 000 peanut butter 500 cottonseed (cooking) oil 350 brown sugar 500 and milk powder 250 parts respectively the poison is a mixture of zinc phosphide 2 parts and calcium carbonate 1 part and is added in such amount that the bait will contain 0.75 per cent of zinc phosphide

In built up areas traps should also be used and buildings should be made rat proof It is important to try to prevent the establishment of the Norway rat and to prevent the introduction of diseased rats and for this purpose poisoned bait and traps are used in the dock areas.

The results already obtained indicate that the rats could be much reduced in numbers but not exterminated by these methods

J F Corson

TANGANYIKA TERRITORY DAR ES SALAAM SURVEY DIVISION DEPARTMENT OF LANDS & MINES Atlas of the Tanganyika Territory With Foreword by H P ROWE (Chief Surveyor Director of Civil Aviation and Controller of Aerodromes) 29 pp 1942. Dec. [50s]

The Survey Division of the Department of Lands and Mines and those who collaborated with them are to be congratulated on an admirable feat of cartography in the production of this atlas The features which it is desired to display in the various maps are very easily and clearly appreciated by the reader there is no fumbling in the drawing and the paper is of fine quality

The maps (on 29 pages each measuring 17½ in. x 17¼ in.) show the physical features rainfall temperature etc. but for readers of this *Bulletin* particularly interesting are those which show the distribution of tsetse and sleeping sickness malaria, medical facilities population and communications. An attractive feature is the Historical Section in which maps dating from the time of Homer to the end of the XIX century are reproduced. At the end is a map of the routes taken by some of the European explorers beautifully drawn

Charles Wilcocks

HADDOW A J On the Mosquitoes of Bwamba County, Uganda I Description of Bwamba, with special reference to Mosquito Ecology *Proc Zool Soc London* 1945 Oct v 115 Pts. I & II 1-13 2 figs. [28 refs]

The isolation of the yellow fever virus from a human case and from *Aedes (Stegomyia) simpsoni* Theo in Bwamba County Western Uganda in 1941 led to the beginning of an intensive mosquito survey of the area in 1942. This survey is still proceeding and results obtained so far are discussed in Part II of this paper (below)

Part I is concerned with a description of the topography and vegetation of the area the zoogeography of the mosquito fauna and the behaviour of mosquitoes in forest areas

The Commissioners point out that "The detailed story which has to be told and our critical reviews do not lend themselves readily to summarization. The same limitations apply to anyone who attempts to review this tragic report.

Since the terrible famine in 1769-70 in which 10 million of a population of 30 million are said to have died, Bengal had been almost entirely free from famine till 1943. For more than 40 years India as a whole had escaped from great famines—these had come to be regarded by many as things of the past so that the sight of thousands of victims of starvation in the streets of Calcutta came as a great shock to the public in India. The Commission estimated that the absolute shortage of the rice supply available in Bengal in 1943 was of the order of three-weeks requirements—this was a surprisingly small deficit in view of the widespread starvation that resulted. The Commission believed that the shortage of rice and the disturbed conditions due to the war would not have caused a disastrous famine if the Governments of Bengal and India had taken resolute action at an early stage to ensure equitable distribution of the available supply. Equal blame is attributed to certain sections of the public of Bengal—an atmosphere of greed and panic caused a rise in prices to levels which placed rice beyond the reach of the poorer classes. It was estimated that every death in the famine was balanced by roughly 1,000 rupees of excess profit acquired by the dealers in rice. There was also widespread corruption and a moral and social breakdown on the part of some sections of the community.

Less than two pages out of the 107 in the first part of the report are allotted to a description of the background against which the events which led to widespread starvation in 1943 must be viewed, but these pages are of outstanding importance because they contain a clear statement of the basic causes of the famine as opposed to the causes that precipitated the tragedy—they show that the people of Bengal and of many other parts of India were becoming progressively more vulnerable to the effects of any temporary reduction in the food supply.

It is stated that 7½ million families in Bengal are wholly or mainly dependent on agriculture for their livelihood, that less than 2 million of these hold more than 5 acres each, and that about one-half of them hold less than 2 acres or own no land at all. The general consensus of opinion endorsed by the Land Revenue Commission of Bengal, is that 5 acres would be the minimum area required to keep the average family in reasonable comfort and that for some types of land 8 acres would be needed.

As evidence of the previous nutritional condition of the people the commissioners quote the findings of the reviewer who in 1933 carried out a rough but illuminating survey of certain aspects of life in rural India. This survey was based on the personal observations and opinions of large numbers of dispensary doctors in agricultural villages. These findings are regarded by the Commission as indicating in a general way the unsatisfactory state of nutrition of the people of rural Bengal 10 years previous to the famine. "The doctors in Bengal reported that only 22 per cent. of the population were well nourished and that 31 per cent. were very badly nourished. The following further opinions are expressed on this subject—"Poverty and malnutrition left a section of the population with few reserves material or physical to meet superimposed calamity. For them there was no margin of safety and little possibility of tightening the belt. The fact that such conditions are common to most other provinces of India, which escaped the famine, does not detract from their fundamental importance. Agricultural production was not keeping pace with the growth of population. A considerable section of the population was living on the margin of distress.

In a separate Minute Mr M Afzal Husain one of the commissioners states that since 1933 there has been no increase in food production but a steep rise in population he quotes Dr Aykroyd as having estimated in 1943 that for India as a whole there is at all times serious under nourishment of about one-third of the population and goes on to ask why no attention was paid to the warnings given by numerous investigators on economic agricultural medical and nutritional problems.

The second part of the Report deals with death and disease the official figures show that in the second half of 1943 the number of deaths exceeded the quinquennial average by nearly 700 000 and in the first half of 1944 the excess was over 422 000 These figures are admittedly unreliable In the worst areas 10 per cent. of the people died but all over the province the death rate was much higher than normal. Deaths among infants under one year of age were 26.8 per cent. fewer than normal this surprising reduction was due chiefly to a fall in the live-birth rate which fell from 28 to 18.8 per mille but here again the registration of births and deaths is likely to have been more inaccurate than usual

The mortality curve followed the same general trend as in normal years reaching its highest point in December but of course the level was much higher In May and June 1943 the death rate in the province had already risen to a considerable degree from September to December it rose steeply In the early stages of the famine a high proportion of the deaths resulted from starvation later on epidemic diseases especially malaria and cholera, were the actual causes of most of the deaths

Vitamin-deficiency diseases and pneumonia were far less frequent than had been expected. The medical aspects of death from starvation are being investigated separately so that little is said of them in the Report

The quinine situation was extraordinary in November 1943, about 43 000 pounds of quinine were available in Bengal, but distribution was exceedingly difficult the price on the black market was R.300 a pound so that supplies had to be sent under armed escort to the districts In spite of this precaution the Director of Public Health stated publicly in December 1943 that a vast amount of the quinine issued by Government had gone into the black market Eventually quinine and mepacrine became available throughout the province. In 1943 79 000 pounds of quinine and 20 000 pounds of cinchona febrifuge were allotted to Bengal in 1944 65 000 pounds of quinine 30 000 pounds of cinchona febrifuge half a million ampoules of quinine and 382 million tablets of mepacrine were supplied. Large quantities of sulphaguanidine and vitamin preparations including a million capsules of halibut liver-oil presented by Boots Pure Drug Co. were distributed.

Vaccination against smallpox and inoculation against cholera were carried out on a huge scale especially during the first half of 1944 when more than 23 million persons were vaccinated and more than 11½ million were inoculated.

The last part of the Report deals with food-administration and rehabilitation there is a chapter on protective and supplementary foods it is stated that more meat fish eggs and milk are badly needed The high cost of these articles is mentioned but nothing is said about the practical difficulty arising from the fact that a much larger acreage of land is needed to provide a family with a well balanced diet than to supply enough rice or other cereals to satisfy hunger

The medical relief and public-health services of the province are severely criticized for their failure to take effective action during the early stages of the famine when much could have been done to save the situation The medical personnel had not been severely depleted by war conditions except



for the withdrawal of most of the few members of the Indian Medical Service and Indian Medical Department still remaining in Bengal.

The District Health Officers were poorly qualified and poorly paid servants of the District Boards. The standards of efficiency of the medical officers in general are said to have "left much to be desired" discipline and sense of duty were deficient, and morale low."

In pleasing contrast was the efficiency of the medical and public health officers lent by the army in November 1943 these men by their example and precept at once stimulated the subordinate staff to "unwonted activity."

Special praise is given to the young Indian Medical Officers the excellence of their work is said to have been a striking testimonial to the value of their military training.

The formation of a provincial cadre of District Health Officers is stated to be an immediate necessity. The control of these officers by local bodies is regarded as being largely responsible for their failure.

(This remarkably frank and outspoken Report deals exhaustively with the circumstances which precipitated the famine in Bengal. Surprisingly little space has been allotted to the basic conditions—referred to as the "background"—which rendered Bengal so susceptible to famine that a relatively small shortage of the normal food supply was enough to cause the tragedy. The significance of these conditions has not been overlooked by the Commission, who describe them as being of fundamental importance and add the ominous comment that they are common to most of the other provinces of India. It can, therefore, be expected that this aspect of the problem will receive full consideration in the further report dealing with the second part of the terms of reference, which is — *The development of agriculture and the raising of the standards of nutrition so as to make recurrence of famine impossible*." In this term of reference the Commission has been asked to find a solution for the greatest of all the problems that affect the lives and health not only of the people of Bengal and the rest of India but also of more than half the population of the whole world.

The solution would be simple if the inhabitants of the overcrowded countries could be induced to take into account the rigid principle that the greatest quantity of food that can be provided will not be enough for an unlimited number of persons. In these countries reproduction is allowed to occur at the natural rate and this is so high that apart from the checks imposed by premature deaths due to the preventable diseases caused by infection and dietary malnutrition, the population would double and redouble itself every 25-30 years.

It follows that if complete success is to be achieved in the control of infectious diseases and in securing freedom from want and if at the same time no check is applied to the natural birth rate it will be necessary to provide for a corresponding increase in the food supply. In Bengal for example where an immediate increase in the food supply by 50 per cent. is needed it would be necessary to provide this and a further progressive increase reaching three times the present amount by the end of 25-30 years. Six times the present supply would be needed 50-60 years hence and so on.

It is true that some experts have suggested that when people are well fed and comfortable their reproductive capacity automatically declines and therefore there is no need to expect any undue increase in the population. This view finds no support from actual experience of what happens in India where the birth rate is highest in those parts of the country in which food is most plentiful.

Obviously then, in the absence of control of the number of births the balance of population and food supply in the overpopulated countries must be maintained through the slaughter of the surplus population by infectious

diseases or malnutrition. Normally in such countries both of these factors co-operate in a very effective manner.

The balance can be maintained at a pitifully low economic level as happens in the countries in which the average duration of life is less than half as long as it might be—or it can be maintained at a high level of health and comfort as in the countries in which the control of infectious diseases goes hand in hand with the control of the birth rate whether by celibacy, delayed marriage or the use of contraceptives. The last of these methods has created a new problem, race suicide, but the impoverished countries will have ample time to devise safeguards against this eventuality.

The Bengal famine deserves the closest study by all public health workers in overpopulated countries. It shows that a one-sided policy directed solely towards the control of infectious diseases must fail unless it is accompanied by action to ensure an adequate supply of food.

The task that lies ahead of health organizations in these countries is infinitely more difficult and complicated than the one successfully accomplished in progressive countries whose inhabitants have themselves dealt with the food and population problem and so have provided conditions in which the control of infection has achieved astonishing success.] *John W D Megaw*

**COLONIAL OFFICE** Report of the Committee on the Training of Nurses for the Colonies [RUSHCLIFFE Chairman] Cmd 6672. 65 pp. 1 diagram. 1945 Aug. London. H.M. Stationery Office. [1s.]

In November 1943 the Secretary of State for the Colonies set up a Committee under the chairmanship of Lord Rushcliffe to examine the question of training both in this country and overseas for nurses who are to serve in Colonial territories and to make recommendations having regard also to the need in those territories for increased public health activities and for the fostering and developing of community welfare.

The Committee was composed of members with special knowledge and experience of the training of nurses in Britain and also of those with special knowledge of the colonial requirements.

The report which was published in August 1945 is an eminently practical document not only making general recommendations but also giving many detailed suggestions as to how these recommendations might be carried out.

In the main body of the report are given—firstly, accounts of the history and present position of nursing in the Colonies and of the general medical policy there; secondly, recommendations on how training of local nurses might be provided in the Colonies and on how the training of nurses in Britain might be organized so as to enable them to fulfil their task of developing the local nursing services satisfactorily; thirdly, suggestions as to how the recruitment of nurses might be improved and the conditions of service for nurses made more attractive.

In the appendices examples are given of types of legislation and of methods of organization which have been found useful in Britain or in some of the Colonies. Detailed syllabuses for the training of different types of nurses are included. These should prove useful not necessarily for complete adoption but as suggestions for local development. The Committee emphasizes throughout the report the need for research into the most suitable methods of training to suit the local conditions.

The first recommendation in the report is that Representative Nursing Councils and Midwives Councils (or possibly a joint Nursing and Midwives Council) should be set up in each Colonial territory or group of territories. These are for the purpose of controlling and guiding the ordered advancement

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of the standards of nursing by means comparable to those adopted by such statutory bodies as the General Nursing Council for England and Wales and the Central Victoria Board. These Councils would have the duty among others of maintaining Registers of Nurses and Midwives.

The second recommendation is that "Nurses recruited in the Colonies should be trained locally in training schools. An account is then given of the types of training school required, but the Committee add "Colonial nurses who after qualification show special aptitude, should be given every facility for taking post-registration courses in this country or the Dominions."

It is considered that the minimum period of training for admission to the Register of Nurses should be four years, of which the first three should be devoted to "basic training. In the syllabus suggested for this basic training a thorough and well supervised training in medical and surgical nursing is advocated, but emphasis is also laid on the need for study throughout the course of the preventive and social aspects of nursing.

The fourth year of training should be spent in gaining additional experience either in hospital or in midwifery. The term "Community Nurse" is used in the report to describe the type of nurse who works outside the hospital among the people and whose duties are of a dual nature combining those of a Health Visitor and a District Nurse. It is considered that this type of nurse should be of great value in the Colonies where so many of the people live in rural areas and where so much educational work in health matters is required.

Other points to be noted are — The recommendations that Assistant Nurses should be trained and registered in the more advanced Colonies that in backward areas especially in Colonies where two standards of education exist, two grades of nurses should be trained, the aim being to use the lower grade nurses for work among their own peoples and to raise the standard of training year by year up to the higher grade. In training these nurses the combined efforts of educational and nursing teachers are required. Throughout the report this need for close co-operation between the educational and medical departments is stressed, and the interesting suggestion is made that as an experiment there might well be set up joint training colleges of residential type comprising student nurses and student teachers and possibly other vocational students.

In the section dealing with the preparation of nurses in the United Kingdom and the Dominions for work in the Colonial Nursing Service should be given a special course of instruction to equip them more adequately for service in Colonial conditions. This course it is thought, should be of about three months duration, and a very detailed syllabus for such a course is given. The Committee state that they would welcome any increase in the preventive outlook during training of nurses in Britain.

The report ends with a useful summary of the main recommendations.

SIGNORS James Stevens B.S. M.D. Ph.D. Dr. P.H. Sc.D. (Hon.) etc.]  
 M.D. Dr. P.H. HORACE HAROLD MacLACHLAN (B.S. M.D. etc.) &  
 Collaborators Global Epidemiology A Geography of Disease and Sanitation.  
 Volume 1 Part 1 India and the Far East. Part 2 The Pacific Area.  
 pp. xxvi—504 32 maps 1944 London William Heinemann, Ltd. [30s.]  
 [Review appears also in *Bulletin of Hygiene*]

Experience of war especially of war in tropical countries, has always shown that one of the chief difficulties of a commander is the maintenance of the health of his troops. Examples need not be multiplied, but the notorious

records come to mind—the Walcheren expedition of 1809 the French occupation of Haiti in 1800 the Crimean war the Gallipoli Macedonia and Mesopotamia campaigns of 1914–18. In the war which has recently ended troops have been sent to some of the most unhealthy parts of the world and disease incidence has not been low but in most of the campaigns though there have been some surprises not least of which has been scrub typhus the military authorities have at least known what the risks were. Steps were taken to acquire in advance knowledge of the diseases indigenous to the areas to which troops were moved. In the United States a large number of medical men and women were associated with the Intelligence Revision of the Office of the Surgeon General of the United States Army and these collected a considerable amount of information either from personal experience of the countries concerned or by the laborious process of consulting reports or papers in the world medical literature. The reports they made have been brought together and in this volume those dealing with India and the Far East and with the Pacific Area are now published. The editors remark that the authors do not regard this work as final. They would have preferred to delay publication until scrutiny under the more leisurely conditions of peace could have been carried out but have consented to publication at this time because so much of the material is of immediate value to many interests and is not readily available elsewhere.

The countries described are—*India and the Far East*—Burma Ceylon China Formosa, Indo-China India Japan Korea British Malaya Nampou and Ryukyu Islands Thailand. *The Pacific Area*—Australia Cook Islands and Niue Easter Island Fiji French Oceania, Gilbert Ellice Ocean and Nauru Islands Guam Hawaii Japanese Mandated Islands Johnston Island and Northern Line Islands Netherlands East Indies New Caledonia New Hebrides New Zealand North Borneo Sarawak and Brunei Papua New Guinea and the Bismarck Archipelago Philippines Phoenix Islands Pitcairn Samoa Solomons Tokelan and the Tonga Islands.

In each case notes are given of the climate the health services and medical facilities and the common diseases. There is a bibliography for each section and at the end, a series of world maps showing the distribution of certain diseases. The general index is good.

It is evident that information of this kind has as great a value in peace as in war. No similar publication on this scale has previously been issued and though no doubt in future an even greater amount of detail will be required the information now made available will be welcomed. It may, perhaps stimulate some countries, from which annual medical reports are not now issued, to contribute regularly after the fashion set by others who do so report, to the orderly mass of world medical information. Volumes of this kind soon become out of date and the issue of new editions at reasonably frequent intervals will be a task for the future.

The reviewer has had some experience of the labour of compiling reports of this kind [see the reports on the Far East in this *Bulletin* 1944 August to December] and this entitles him to say that this American team has done its work well.

Charles Wilcocks

MEYER MAY, J with the collaboration of HO-DAC DI VU-DINH TUNG  
TONG-THAT TUNG & DINH VAN THANG *Chirurgie tropicale d'urgence.*  
[*Urgent Surgery in the Tropics.*] Préface de M. le Professeur MONDOR  
pp vi+286 9 coloured pls. & 16 figs 1940 Paris Masson & Co  
Editeurs, 120 Boulevard Saint-Germain. [20s.]

This work published in 1940 is based on the author's experience whilst Professor of Surgery at the Medical School at Hanoi in Tonking from 1936 to

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ELLIOTT (p. 278) reports three cases of yellow fever in white soldiers in West Africa. All the patients had previously been vaccinated, but two of them died. Nevertheless the low incidence of the disease is good evidence of the value of vaccination.

KIRK and BATOURI (p. 374) report the first fatal case of yellow fever to be recorded in a European in the Sudan. Non fatal European cases some extremely mild, have been seen there before, and there have been many fatal cases in the Africans of the country.

### Aetiology

STÉFANOPOULOU and DUVOLOV (p. 208) show that yellow fever virus, after prolonged maintenance in tissue culture may undergo marked deterioration in both virulence and antigenic power. A strain of virus 17D which had become attenuated in this way was reactivated by passage through the brains of mice. It did not become pathogenic for monkeys but produced immunity in them. After being cultivated in developing eggs, this strain was then used for vaccination of man, with success.

JACOBS (p. 485) has shown that in a mixture containing 10 per cent. human serum and 0.4 per cent. sodium chloride to which is added ammonium sulphate to 1 per cent. strength, at pH 6.3-6.5 yellow fever virus remains viable at 22-25°C., for as much as 20 days. Simple saline solutions are rapidly lethal to the virus, and the addition of serum is at best not very effective in preserving it.

LIMARES (p. 277) shows that young cats are relatively unresponsive to yellow fever. He (p. 278) has been able to infect young mice by instilling the virus into the nostrils the ear on to the scarified cornea into the stomach, or even by rubbing it into intact or scarified skin. The same author (p. 278) shows that chicks are susceptible to yellow fever virus injected by various routes and that the virus persists longer in the brain than in the other organs. Virus may be present in the brain, and at the same time immune bodies may exist in the blood.

LIMARES (p. 373) has found that filtrates of cultures of *Aspergillus flavus* *Penicillium camemberti* and a species of *Actinomyces* have a lethal effect on the yellow fever virus both *in vitro* and *in vivo*. A mixture of filtrate and virus is not pathogenic to mice and injection of filtrate into these animals protects them against injection of virus several hours later. A non infective mixture of filtrate and virus however possesses antigenic properties and stimulates immunity.

### Transmission

CORON (p. 597) has compiled, from the extensive literature on yellow fever transmission, a list of vertebrates tested for susceptibility to the virus of fever, in which vicerotropic virus has been shown to persist, and of blood sucking arthropods on which transmission experiments have been made. This list has been made as complete as possible and brings the information up to date.

HECHT and ANDRUZ (p. 463) give an account of the mosquitoes of Bolívar State Venezuela, in so far as these may be concerned with the transmission of yellow fever. Special attention was paid to the jungle mosquitoes. [An examination of the table quoted by these authors from an earlier work, and showing the mosquitoes capable of transmission or in which virus has been found reveals certain errors which have crept into the literature see p. 640.] BOSHELL, MARRIOTT and OSORIO-MESA (p. 114) have demonstrated the existence of yellow fever virus in *Haemagogus capricornis* and (probably) *Aedes*

*Leucocelaenus* captured in uninhabited jungle in Colombia. Protective antibodies were found in certain marsupials. *Haemagogus capricornis* is attracted to light travels considerable distances from its breeding places and tends to follow man and mules some distance from the forest.

BEVIER (p 557) contributes a report on the yellow fever service of British Guiana. No case was discovered in the year 1944. The supervision of air craft and railway trains showed that there was a considerable transport of mosquitoes able to convey yellow fever and other diseases.

It is well known that *Aedes aegypti* breeds in fire buckets flower vases in cemeteries drinking troughs and similar small collections of water. CHANDLER (p 32) claims that phenothiazine is the ideal substance for control of such breeding and that it may be applied as a powder or incorporated in glue on small squares of paper which are placed in the water or as a suspension in dilute alcohol. A single application in the proportion of 1 part to 60 000 of water will prevent breeding for three months or more.

HENDERSON (p 374) describes the steps by which a high breeding rate of *Aedes aegypti* in Savannah (on more than one-third of the premises) has been reduced so that it now occurs on no more than 2 per cent of premises.

### Immunity Clinical Features

By a series of carefully planned experiments LINHARES (p 279) has shown that in camondongos [Brazilian house rats] passive immunity (lasting 10 days or so) is transmitted from mother to young *via* the placenta and *via* the milk (lasting as long as lactation continues). Antibodies therefore pass through the placenta and also into the milk. There is no evidence that the virus itself does so.

PERLOWAGORA and LENNETTE (p 114) have studied in animals the complement fixation reaction for yellow fever. The antigen for this reaction appears in the serum on the 3rd to 6th day after infection but the antigen is not directly associated with the virus which may exist in the absence of the antigen. The antibody is present in the serum of animals recently recovered from the disease. The test may be useful in diagnosis of human yellow fever. [For previous work by these authors on this test in which antigen was obtained from infected mouse brain see this *Bulletin* 1945 v 42 83.] The same authors (p 802) have found a correlation between the clinical severity of yellow fever and the amount of complement fixing antigen in the blood whereas there is no fixed relation between clinical severity and the amount of liver damage found after death. Moreover the liver changes usually regarded as characteristic of yellow fever can be produced by injection of tannic acid but without the formation of yellow fever virus antigen. The work indicates that the antigen is specific and it was found in all the animals which had been infected with yellow fever. The complement fixation test therefore constitutes a more accurate and reliable method of diagnosis of yellow fever infection than the histopathological examination of tissue such as liver.

DE ASSUMPCÃO (p 277) discusses the differential diagnosis between yellow fever dengue Rift Valley fever sandfly fever and leptospirosis. In spite of certain similarities—clinical and pathological features transmission by *Aedes* production of lasting immunity—there is no cross-immunity between yellow fever and Rift Valley fever.

SELLARDS and McCANN (p 115) produce evidence that the oral administration of choline hydrochloride in monkeys infected with yellow fever has a protective action on the liver. Five of 8 monkeys so treated survived whereas all of 4 controls died. There was evidence of repair in the livers of those treated monkeys which died.

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## Control

In the Fourth Interim Report of the Inter Departmental Committee on Yellow Fever Control (p 721) are given recommendations concerning the most important measures of yellow fever control, especially with regard to suppression of *Aedes* breeding near aerodromes, ports and other places on transport routes the disinsectization of aircraft, the vaccination of travellers and those working at aerodromes, and the diagnosis of yellow fever. These should be read in the original. In the *Epidemiological Information Bulletin* issued by the Health Division of UNRRA (p 890) are given the standards for manufacture and control of yellow fever vaccine these are stringent. They cannot further be abstracted, and details should be sought in the original. HARGETT and BURRIS (p 803) describe their method of testing yellow fever vaccine by intracerebral injection into monkeys. The vaccine contains no serum and is attenuated but in doses containing high virus content is capable of producing severe encephalitis in the monkeys. These monkey tests are a safeguard to man, and issue for human use is controlled by the results of the animal tests. No ieterogenic or other untoward reactions have been recorded from batches released, after these tests for use in man. SPRAGUE and BARAARD (p 890) report the cases of two men allergic to egg protein who suffered severe reactions after the injection of yellow fever vaccine and typhus vaccine respectively. They advise that such persons should be excluded from the Services. Charles Wilcocks

## MALARIA.

OSGOOD S B Malaria and the Returning Soldier J Amer Med Ass  
1945 June 16 v 123 No 7 512-13

Two persons, a white girl and a white woman, living in the State of Oregon U.S.A., apparently contracted benign tertian malaria from a soldier who had returned from the Pacific area. *Plasmodium vivax* was found in the blood in all three people. The girl and woman lived near a creek where mosquitoes were numerous but, according to the official records no malaria had existed the soldier who was related to the girl, had lived in a tent about 50 feet away from her house for over two weeks before she got the attack, and had often passed near the woman's house. Mosquitoes caught near the girl's house were identified as *Anopheles punctipennis* and *Culis tarsalis* and six specimens caught in the woman's house were *Anopheles maculipennis*. The presence of anopheline vectors of malaria in this neighbourhood had not been suspected. There may have been a third case in a logging partner of the soldier he was said to have had chills and fever but could not be found for examination.

MELVILLE A. R. WILSON D Bagster GLASGOW J P & HOCKING K. S  
Malaria in Abyssinia. East African Med J 1945 Sept, v 22, No. 8  
285-84 1 map (10 refs.) J F CORSON

A Mobile Malaria Section of the East African Army Medical Corps carried out malaria surveys in over 50 localities in Abyssinia during the British occupation of that country in 1941-42. Some of the results of these surveys are here recorded. The Rift Valley traverses Abyssinia from the north of Lake Rudolf north-eastward to the Red Sea. A *gambiae* the chief vector was found throughout

the valley. Other species of *Anopheles* found in the Rift Valley were *A. coustani*, *A. obscurus*, *A. ardensis*, *A. kingi*, *A. d'thali*, *A. demeilloni*, *A. gambiae*, *A. macmahoni*, *A. christyi*, *A. cinereus*, *A. pretoriensis*, *A. maculipalpis*, *A. pharoensis* and *A. squamosus*. Of these species only *A. pharoensis* and *A. d'thali* demand serious consideration as possible vectors. *A. pharoensis* is very common over wide areas, enters human dwellings and bites readily. The few dissections made revealed no sporozoites. This species was always found in association with *A. gambiae* and thus no circumstantial evidence was available as to its potentialities as a vector. *A. d'thali* is strongly suspect. It occurs in the Red Sea littoral. It was the only species found at Mordale (700 metres) where malaria occurs.

*A. gambiae* was found to be the vector of epidemic malaria in places in which mosquito breeding was dependent on rainy seasons. In other places the species was present throughout the year, breeding in residual pools left in river beds after torrents had subsided. In some of the smaller permanent rivers, pools and gently trickling water provide facilities for *A. gambiae* breeding.

As the level of the country falls from the plateaux of the east and west to the floor of the Rift Valley, malaria endemicity increases till a zone of moderate hyperendemicity is reached between 1,500 and 1,800 metres. At lower levels there may be intense hyperendemic malaria near streams, rivers or lakes, or low endemicity where rainfall is small. In the latter places malaria is essentially seasonal.

Much of Abyssinia north-west of the Rift Valley is free from malaria, most of the country over 2,000 metres being too cold. There may be annual or periodic epidemics of malaria of some severity in this high country, but the endemicity and severity of epidemics are lower than in the Rift Valley. *A. gambiae* is the chief vector here also. At Jimma *A. funestus* was found in fair numbers after the rains and when the swamps had fallen in level. Other *Anopheles* found in the north-west were *A. coustani*, *A. kingi*, *A. nili*, *A. marshallsi*, *A. harperi*, *A. demeilloni*, *A. christyi*, *A. cinereus* and *A. squamosus*.

South-east of the Rift Valley, a massive mountain range forms the watershed of the Juba and Uebi Scebelli Rivers. East of this the land slopes to the low deserts of Somalia. Malaria occurs in varying degree along the slopes of the Chercher mountain range. Transmission is either absent or very brief at Harar (1,930 metres). There are highly endemic areas near Lake Chercher. At Negelli (1,290 metres) malaria transmission is slight and seasonal. Low endemicity characterizes the area including Mega, Moyale, Adola and Ghimir, with the exception of the Dawa, Parma and Ganale Doria river valleys, which are highly malarious. *A. gambiae* is the malaria vector in this south-east area. Other species found were *A. coustani*, *A. lesoni*, *A. rhodesiensis*, *A. demeilloni*, *A. cinereus* and *A. pretoriensis*.

Norman White

THOMSON R. C. M. Studies on the Breeding Places and Control of *Anopheles gambiae* and *A. gambiae* var. *melas* in Coastal Districts of Sierra Leone. *Bull. Entom. Res.* 1945 Sept. v. 36 Pt. 2, 185-252, 8 text figs., 48 figs., on 13 pls. & 8 maps. [27 refs.]

*Anopheles melas* (for in the text the author accepts RIDBANDS's view that this is a species rather than a variety [this *Bulletin* 1945 v. 42, 3]) differs from *A. gambiae* not only in the characters described by that author but also in the egg. This has a broad upper surface with the space between the frill and the float so narrow that they appear to be in actual contact instead of the narrow upper surface with a distinct space wide enough to show the polygonal marking of the chorion between the frill and float in *A. gambiae*. The distinction of the



two species on the palpal bands is indefinite. *A. melas* sometimes having three and sometimes four bands and the proportion with each number varying from place to place.

The use of this characteristic has made it possible to identify with certainty the breeding places of the two species. *A. melas* is restricted to coastal areas and brackish swamps, very rarely making use of fresh water. Of 2,647 eggs collected from fresh water unaffected by tides, only 30 were of the *melas* type and these were found in places close to its normal breeding areas.

Breeding of *A. melas* is confined to the stretch of ground between high neap-tide and high spring tide levels, and there only occurs in association with certain flora. *Avicennia nitida* mangrove and sea grass or *Paspalum* Mangrove is of two types the very common *Rhizophora racemosa* with the well-known characteristic of roots like the staves of an inverted umbrella, and *Avicennia nitida*, which resembles an apple tree in appearance. The former is very much the commoner and grows in mud below neap-tide level the latter grows in scattered isolated "orchards," always above neap-tide and below high spring tide level, on ground which is fairly solid and covered with a mat of leaves, but with many pools. On the extreme inland side of mangrove areas of whichever type, there are often areas of sea grass which are inundated by extreme tides and which on account of their position tend to receive also fresh water from seepages as well as from rain. In *Avicennia* orchards, egg laying takes place on the earliest of the spring tides often only on the shore side of the orchard, and the eggs are distributed by the action of the tide, they and young larvae being undamaged by tidal water which may flood the entire area to a depth of a couple of feet. On the subsidence of the spring tides some eggs are left in pools, in which they develop others are stranded in mud, in which they survive until the next series of high tides floats them, when the eggs immediately hatch. In consequence the output of adults is highly periodic, occurring in waves a few days after the end of the spring tides. In *Paspalum* areas egg laying may occur at any time, but is in fact often periodic as a reflexion of the varying numbers of adults available to lay. The periodicity and size of the output of adults is dependent on the following factors:—(a) the occurrence of spring tides (b) the periodicity of the tides, as in a single month there may be either one or two series of sufficient height to flood the *Avicennia* orchards (c) the occurrence of rain in sufficient amount to prevent the pools left by spring-tides from drying up before larval development is complete and (d) the presence of seepages maintaining tidal pools, especially in *Paspalum* areas. These factors react together in different ways in different places and at different seasons, but in general, output is greatest in the rainy season, particularly in June when it may be enormous and continues until some months after the end of the rains, when seepages dry up and reaches its lowest levels in the months of January to April. Although egg-laying only happens in coastal brackish water a laboratory experiment suggests that it is not itself dependent on salinity, and the factor which causes this mosquito to choose this type of breeding place is not understood.

*Avicennia* orchards can be detected from the ground only with great difficulty. They are more readily detectable from above from a nearby hill if such exists or from aircraft. This last is the best method as accurate mapping can be done by aerial photography which has revealed only 17 orchards, many of them minor in the enormous extent of general mangrove in the Free town estuary. Control by drainage is not effective as opportunity for egg-laying and for the persistence of some breeding pools, inevitably occurs after spring tides. Control by embankment to exclude the spring tides from areas of *Avicennia* and *Paspalum* associated with drainage of fresh water through tide gates is much the most successful and completely eliminates breeding.

A summary of dissections by another worker and of which it is said that a detailed report will be published later shows that 42 of 1 000 salivary glands contained sporozoites and 44 of 931 (4.7 per cent) stomachs contained oöcysts the total infection rate being 7.3 per cent.

*A. gambiae* of the type form breeds in fresh water pools exposed to the sun. Detailed analysis of breeding places and of places not selected for breeding shows that this is only a small part of the story and much remains obscure. Of the apparently suitable pools available only a very small proportion are utilized but these often contain very numerous larvae and continue to do so for long periods and generalizations on breeding habits are impossible or at least dangerous. In the general attack on a type of breeding place it is not uncommon to treat numerous water areas which are in fact harmless and to overlook a few small ones which provide almost the entire local adult mosquito population. Breeding commonly occurs in small pools in sweet potato patches and prolifically in rice fields at all stages of cultivation and throughout the entire season but not throughout the entire extent of the field. In the rainy season profuse breeding occurs along the edge often only a fraction of it. In the dry season though the water area is diminished breeding becomes more widespread and the total output of adults may increase. Field trials show that oviposition is not influenced by light and shade or by salinity below 30 per cent of sea water or by surface films caused by iron bacteria (though these films when continuous may prevent larval growth) but is influenced by mechanical obstruction interfering with the flight of the female before oviposition as is the case with *A. culicifacies*.

*A. nili* has not in the past been regarded as an important vector of malaria in Sierra Leone but it is here shown that in the dry season it may be the most abundant anopheline in some villages and may have very high sporozoite rates. GORDON *et al* [this Bulletin 1933 v. 30: 301] found a sporozoite rate of 9.1 per cent and TREDRE is reported as finding one of 3.2 per cent. It must therefore be considered as an important carrier of malaria.

[This paper contains much statistical and geographical information which cannot be adequately indicated in a review and is illustrated by 50 photographs as well as by maps and plans. Any worker concerned in the control of *A. gambiae* in any part of Africa should try to see it in the original.]

G Macdonald

DELVILLE J. Infection naturelle d'*Anopheles demeilloni* par oöcystes de plasmodium. [Natural Infection of *A. demeilloni* with Plasmodial Oöcysts.] *Rec Trav. Sci. Méd. Congo Belge* 1945 July No. 4: 112.

The author has found oöcysts (probably of *P. falciparum*) in one specimen of *Anopheles demeilloni* captured in Ruanda.

CAMBOURNAC F. J. C. & SIMÕES J. M. P. Sobre a produção de *Anopheles* nos arrozais de Aguas de Moura. [The Production of *Anopheles* in the Rice-fields of Aguas de Moura.] *An. Inst. Med. Trop. Lisbon* 1944 Dec. v. 1 No. 2: 229-39. 2 graphs.

In a previous publication the senior author described his method for determining the larval *Anopheles* population of rice-fields [this Bulletin 1939 v. 38: 920]. The interesting observations then reported have been continued during four successive rice-growing seasons and the results of those observations are here recorded. Malaria is hyperendemic in the Aguas de Moura district. *A. maculipennis atroparvus* is the only vector. *A. claviger* also occurs breeding

in clear cool water but it is scarce and associates neither with human beings nor with domestic animals. It is of no importance as a vector of malaria.

Breeding of *A. m. atroparvus* is at its maximum in May and June. There was considerable mortality among the larvae of all instars which did not appear to be due to an increase of their natural enemies. The proportion of the various instars in the total catch varied with great irregularity. The complete or almost complete absence of pupae after the end of June was a constant and striking phenomenon though larvae in the fourth instar could be found. In the earlier months when pupae were found, their numbers had no constant relation to the numbers of fourth instar larvae. Though the production of adult anophelines ceases at the end of June the number of these insects in catching-stations remains high throughout July and August. This indicates that the length of life of adult *A. maculipennis atroparvus* in natural conditions is from one and a half to two months.

It is estimated that at the height of the breeding season each hectare of rice fields is capable of producing from 30 000 to 35,000 anophelines a day.

Norman White

EICHLER, W. Anopheles-Beobachtungen in Griechenland. [Observations on the Anophelines of Greece.] *Deut. Tropenmed. Ztschr.* 1944 June, v 48, Nos 11/12, 261-72, 9 figs.

PERRET-GENTIL, A. L'observation des réfugiés malarieux dans la section clinique et le laboratoire de l'Institut Tropical Suisse. [Study of Malaria among Refugees carried out in the Clinical Section and the Laboratory of the Swiss Tropical Institute.] *Acta Tropica* Basel. 1945 v 2, No. 2, 97-121 10 figs.

The arrival in Switzerland of a large number of Italian and Yugoslav refugees infected with malaria provided an opportunity for the staff of the Tropical Institute at Basle to undertake an intensive study of a disease that is rare in Switzerland. Very full advantage was taken of this opportunity. This paper records the results of the study of some 185 cases of *P. vivax* malaria.

Apart from the attacks of fever characteristic symptoms were but little in evidence. Pain in the legs was a frequent complaint. Some temperature charts were very atypical. In about a quarter of the cases the fever was quotidian. Often a loss of weight heralded a relapse. In cases in which no merozoites were found in the peripheral blood the injection of certain provocative agents sometimes yielded good results: adrenaline, milk, Caseosan and Pituit. glandol were used for this purpose.

In the examination of blood a method is described which gave better results than the thick drop method. Four or five smears are superimposed, each smear being dried by waving the slide in the air before the next smear is spread.

Observations indicated that *P. vivax* has a greater affinity for mature red cells than for reticulocytes. Difficulty was sometimes experienced in differentiating the basophil stippling of red cells from Schöflner's dots in their early stage. Sternal puncture was not more successful in revealing parasites than was the examination of the peripheral blood. Henry's reaction was of little value.

In treatment intravenous injections of quinine-calcium were often used without giving rise to any untoward symptoms. A preparation Calguquine Sandoz in particular proved an active remedy that was well tolerated. Vitaquine Roche in tablet form gave results equal to those given by the usual quinine preparations.

Norman White

WILSON Margaret E & WILSON D Bagster Malarial Infectivity in African Soldiers in a Hyper-Endemic Area *East African Med J* 1945 Sept v 22 No 9 295-7

During a period of six months thick blood films were taken fortnightly from 137 African soldiers who were being exposed to frequent reinfection by alien if not new strains of malaria parasites. The results of the examination of these films are recorded. None of the men was sick when the films were taken. The men belonged to a large variety of tribes and most had a considerable degree of immunity to malaria. They were classified as immune 76 semi-immune 42 non-immune 19.

The average parasite rate at these examinations was 16.1 per cent. *P. falciparum* 14 and *P. malariae* 2.1 per cent. Crescents were counted against leucocytes or when very few recorded as one or two in the whole thick film. Only three crescent carriers were found with counts of over 10 per 500 leucocytes, two of them being of non-immune tribes. Eight had counts of 1-4 per 500 leucocytes. Twenty-eight crescent carriers had counts of less than one per 500 leucocytes. On the assumption that at least one crescent per 500 leucocytes is necessary for successful mosquito infection not more than 1 per cent of these soldiers at any one time was a probable infector. Half of these infectors belonged to the non-immune group which formed but one seventh of the men examined.

Norman White

FREDERICKS M G & HOFFBAUER F W A Study of Hepatic Function in Therapeutic Malaria. *J Amer Med Ass* 1945 June 16 v 128 No 7 495-8 4 charts [13 refs]

Thirty-one patients subjected to malaria therapy are the basis of this report. 21 men and 10 women between 28 and 62 years of age. All suffered from acquired neurosyphilis. *P. vivax* was inoculated intravenously in 29 intramuscularly in 2. No manifest liver disease was noted in any of these patients before submission to malaria therapy. All but six of the patients received general diets, the six received liver-sparing diets, high carbohydrate, high protein and low fat.

Among the clinical features recorded were loss of weight, symptoms and signs of gastrointestinal disturbance, degree of weakness. Hepatic disturbance was assessed by the quantitative serum bilirubin test, the cephalin cholesterol flocculation test, the amount of urobilinogen in the urine and the sulphobromophthalein dye retention test. The technique of these tests is briefly described. The results obtained are recorded in the form of graphs.

All the patients showed some evidence of hepatic dysfunction, there was jaundice in one patient, enlargement of the liver in four and spider naevi in five, symptoms which correlated with the hepatic disturbance revealed by liver function tests. The weight loss during and immediately after malaria therapy was striking, this can be lessened but not prevented by special diet. More attention should be given to the study and use of protective diets during malaria therapy. Such therapy is admittedly contraindicated in the presence of clinically manifest hepatic disease.

Norman White

CHEN K. T. TANG I. L. & WANG M. C. Congenital Malaria. Report of a Case. *Chinese Med J* Washington D.C. 1944 Apr-June v 62 No. 2 199-205

MARSHALL P. B. Loss of Antimalarial Properties in Quinine Degradation Products. *Nature* 1945 Oct 27 505-6

A degradation product of quinine was obtained by KELSEY *et al* [this Bulletin 1944 v 41, 923] following incubation of the alkaloid with rabbit

**Liver *in vitro*** It was shown by MEAD and KOEPFLI [this *Bulletin* 1945 v 42 8] to be a simple derivative of quinine in which the H atom at position 2 of the quinoline nucleus was replaced by a hydroxyl group. The present author has investigated the action of the degradation product on *P. gallinaceum* infections of chickens. In one incubation experiment half the rabbit liver emulsion with quinine was treated with alkali, in order to destroy enzymatic activity the other half was untreated. The chloroform extract of the former contained unchanged quinine the latter did not. Both extracts made up in HCl, were used in the treatment. The antimalarial activity of the pure degradation product in dilute HCl was also compared with that of a corresponding dose of quinine. It was found that the above extract in which all the quinine had been metabolized, as well as the degradation product isolated in the pure state failed to reduce the number of parasites in the peripheral blood of the chickens. [SILVERMAN *et al* (this *Bulletin* 1945 v 42 448) found, on the other hand, that it was as effective as the parent substance in inhibiting the respiration of the same parasites *in vitro* but affected aerobic and anaerobic glycolysis to a lesser degree.] The author notes that whereas quinine and quinidine are metabolized in the same way cinchonine and cinchonidine are not metabolized by chick liver suspensions. This fact may be of some significance in preparing new antimalarial products of related type.

J. D. Fallon.

**MARSHALL, P. B. & ROGERS, E. W.** A Colorimetric Method for the Determination of Cinchona Alkaloids. *Biochem. J.* 1945 v 39 No 3 258-60 2 figs

1. A colorimetric method for determining cinchona alkaloids based on the formation of a coloured compound with bromothymol blue, is described.

2. Using small capacity cells in a photoelectric photometer the method is sensitive to 0.25 µg. of alkaloid.

3. The specificity of the reaction has been investigated, and lists of substances which do or do not combine with bromothymol blue are included.

**THOMPSON, J. H.** Large Initial Doses of Aisbrine in the Treatment of Benign Tertian Malaria. *J. Trop. Med. & Hyg.* 1944 Dec.-1945 Jan. v 47 No 6 61-4

One hundred American soldiers who had acquired *P. vivax* infections in the Mediterranean area during 1943 were treated for relapsing malaria in England during the following March and April. Seventy-eight of these patients received an initial dose of 0.6 gm. of mepacrine followed by 0.2 gm. after each meal for six doses and then 0.1 gm. thrice daily after meals for 7 days. The remaining 22 patients received 0.2 gm. of the drug every four hours for five doses and then 0.1 gm. thrice daily for 5 days. All the mepacrine was given by mouth in the form of 0.1 gm. tablets. It was always given after meals. If the initial dose was given between meals it was preceded by a pint of chocolate milk, fruit juice or egg nog.

Of the 78 patients who received the large 0.6 gm. initial dose of mepacrine three (4 per cent.) relapsed between 14 and 30 days after completion of treatment. Five (23 per cent.) of the 22 patients on the smaller doses relapsed during the same period of observation. In none of the 100 patients were there toxic symptoms severe enough to necessitate modification of the treatment. Fifteen per cent. had mild abdominal cramp after the initial 0.6 gm. dose 6 per cent. had mild diarrhoea.

The eight patients who relapsed were subsequently treated with still larger doses: an initial dose of 1 gm. followed by 0.2 gm. every 4 hours for 6 doses and then 0.1 gm. thrice daily for a week. This very large initial dose was

given 24 hours after the second or third chill. In four of the cases serial blood smears were taken every 45 minutes after the initial dose. Clumping of the pigment in plasmodia was seen as early as 45 minutes after the initial dose thereafter disintegration became progressively more marked and after about 6 hours destruction was complete. About 6 hours after the 1 gm dose the patients experienced a very violent chill the last and only one. Toxic effects were more in evidence than after the 0.6 gm dose. Four patients had nausea one vomited one had marked diarrhoea and one had mental symptoms. The delirium of the patient with mental symptoms was transitory and may have been due to the fever or mepacrine or both.

Norman White

ANN TROP MED & PARASIT 1945 Oct 10 v 39 No 2 128-32. Prolonged Oral Administration of Mepacrine. I The Effects on Tests of Organ Function. [The Army Malaria Research Unit Oxford (MAEGRAITH B G *et al*)]

Forty three healthy young male adults were given mepacrine 0.1 gm daily. At the beginning of this study careful biochemical examinations were made on each individual. The examinations were repeated at intervals of approximately three months until the end of the experiment which lasted between 9 to 12 months. The findings in the later tests were compared with those of the initial tests and with those obtained with 13 similar subjects who received no drug. No significant change could be observed in the following—icterus index serum bilirubin fasting blood sugar glucose tolerance fructose tolerance blood urea urea clearance hippuric acid synthesis total plasma protein, albumin globulin ratio in the plasma plasma fibrinogen Takata Ara test blood chloride or qualitative examination of the urine. It is concluded that there is no evidence that this course of mepacrine impairs the efficiency of the liver or kidney. [A brief account of these experiments was published in the *Lancet* 1945 Aug 4 141 (see this *Bulletin* 1945 v 42 863)]

F Hawking

ANN TROP MED & PARASIT 1945 Oct 10 v 39 No 2 133-6. Prolonged Oral Administration of Mepacrine. II Haematological Effect. [The Army Malaria Research Unit Oxford (MAEGRAITH B G *et al*)]

Sixty five women and 30 men (all healthy young adults) were given mepacrine in a dosage of 0.4-0.7 gm. weekly for 4-10 months. During this period there was no significant change in the red-cell count the white-cell count the haematocrit or the erythrocyte sedimentation rate. A small rise in haemoglobin concentration occurred in the men taking mepacrine and also in a control group of 14 men who received no drug. This apparent rise may have been due to some alteration in the standard used for measurement rather than to any true physiological change. It is concluded that this dosage of mepacrine for long periods has no deleterious haematological effect. [See this *Bulletin* 1945 v 42, 863]

F Hawking

GAHAN J B & LINDQUIST A W DDT Residual Sprays applied in Buildings to control *Anopheles quadrimaculatus* *J Econom Entom* 1945 Apr v 38 No 2 223-30

— TRAVIS B V MORTON F A. & LINDQUIST A W DDT as a Residual-Type Treatment to control *Anopheles quadrimaculatus* Practical Tests. *Ibid* 231-5

— & LINDQUIST A W DDT as a Residual-Type Spray to control Disease-Carrying Mosquitoes Laboratory Tests. *Ibid* 236-40

This series of papers constitutes a full enquiry into the efficacy of DDT for the control of adult *Anopheles quadrimaculatus* starting with laboratory

experiments and passing on to small field trials and then to large scale field work.

In the laboratory trials cages of various materials were treated with known quantities of DDT anophelines subsequently liberated into them and the knock-down and mortality studied. The knock-down was noted hourly for the first five hours and the final mortality was recorded at 24 hours. Preliminary trials showed that *Anopheles quadrimaculatus* and *Aedes aegypti* were about equally susceptible and anophelines only were therefore used in later tests.

The concentration of chemical in the spray used does not materially affect the toxicity of the residue if the deposit is the same and 2.5 per cent. DDT was used as the standard. The nature of the vehicle did affect its toxicity to some extent emulsions and suspensions being about equal to each other and a little better than kerosene solutions. The lethal effect was slow and exposures of 2 to 4 hours were required to give kills approaching 100 per cent. in the case of newly applied films and as long as 4 hours in the case of older films. The exposure time required for complete mortality was the same 17 weeks after sprays had been applied and increasing the amount of DDT from 50 to 400 mgm. per sq. ft. of surface did not decrease the time.

Unpainted surfaces treated with the chemical remained lethal for long periods, in some cases as much as a year but the knock-down time slowly increased during this time from about 2 hours to 5 or more hours in films 32 weeks old. On painted surfaces a 100 per cent. kill was recorded 32 weeks after 50 mgm. per square foot had been applied to surfaces coated with cold water casein paint. The duration of effect was however much shorter on surfaces recently treated with oil paint, mortalities below 100 per cent. being recorded when the film was a week old and the knock-down after 5 hours being reduced to 25 per cent.

Exposure of treated surfaces to sunlight reduced the length of time for which they were effective by about half and experiments to determine whether mosquitoes left the treated surfaces before they had received a lethal dose showed that the great majority died within 24 hours of voluntarily leaving surfaces treated in this way.

In the field trials rooms were treated with known doses and the effect on artificially introduced or naturally entering anophelines was studied, the dose was varied from 50 mgm. up to 225 mgm. per square foot and resulted in a reduction of the anopheline population to about 4 per cent. of that in control rooms. The duration of effect could not be studied owing to a natural decrease in the control rooms four weeks after the experiment was started. Mosquitoes attempting to leave the rooms were captured and 95 per cent. of those leaving died within 24 hours.

The authors also studied the biting rate of anophelines not yet knocked down in treated rooms and found that this was about proportional to the numbers surviving in the room and concluded that obvious contact with DDT does not act as a deterrent to biting.

In the large field trial, two areas each of about 9 square miles were selected in rice growing country and all buildings bridges culverts and other possible shelters were treated. In the one the average dose was 56 mgm. per sq. ft. and in the other 208 mgm. per sq. ft. and adjacent similar areas served as controls. The object was to see if the general anopheline population in the vicinity of sprayed buildings, as well as in the buildings themselves, could be reduced by the use of residual sprays without employing other methods and this was studied by counting anopheline adults in the treated houses and in nail bags left as traps throughout the area, and also by estimating the numbers of larvae in local breeding places.

The anopheline counts in houses for four months following the end of treatment are recorded in detail and when compared with adjacent control areas showed a reduction of 91 per cent where 56 mgm per sq ft had been applied and of 99 per cent. where 208 mgm had been used. The counts were normally made in the afternoons when mosquitoes would have been in contact with treated surfaces for several hours the few counts made in the early morning showed a smaller relative reduction but as the great majority of captured adults died in 24 hours it may be assumed that these only reflected the previous night's hatch.

The catches in the artificial traps showed no difference between the treated zones and the controls. There were however a number of confusing factors affecting these results and it is not to be taken as proven that there was no reduction in the general mosquito density.

Estimation of the numbers of larvae in breeding places in treated and controlled zones was done by a dipping technique at weekly intervals after the experiment had started. In each of the 20 counts recorded there was a reduction in the treated area which when compared with the controls amounted to 51 per cent. in the zone where 56 mgm. were used and 63 per cent in the zone where 208 mgm had been applied. In each case the number of small medium and large larvae was recorded and it is noticeable that the reduction of large larvae was less than that of small ones.

G Macdonald

DEONIER C C, MAPLE J D, JONES H A, HINCHEY Edna & LIDE P M  
DDT as an Anopheline Larvicide—Laboratory Tests. *J Econom Entom*  
1945 Apr v 38 No 2 241-3

— BURRELL, R. W, MAPLE J D & COCHRAN J H. DDT as an Anopheline  
Larvicide. Preliminary Field Studies. *Ibid* 244-9

WISECUP C. B & DEONIER C C. DDT for the Control of *Psorophora* Mosquitoes  
*Ibid* 250-52.

This series of papers constitutes an enquiry into the effect of DDT as an anopheline larvicide starting with laboratory tests and going on to field studies.

In the laboratory tests early fourth instar larvae of *Anopheles quadrimaculatus* were used and mortality readings were made at 24 and 48 hours after application of the larvicide. In some cases the tests were continued for long periods new larvae being introduced periodically and the effect of rain artificially simulated.

The minimum lethal dose of acetone water suspensions of DDT could not be accurately determined but 98 per cent mortality was seen at a concentration of 0.01 parts per million 55.5 per cent. at 0.005 p.p.m. and some toxicity was shown at 0.00125 p.p.m. It was found to be about 100 times as toxic as phenothiazine and more rapid in action. When applied as a dust and compared with Paris green it was found that doses of 0.005 lb DDT per acre gave 100 per cent kill in 48 hours while 0.1 lb Paris green per acre only gave 85 per cent kill in the same period. DDT had the additional great advantage that it was very resistant to sinking either naturally or after rain its resistance was always obvious but to some extent depended on its physical form. micronised DDT surviving 14 to 20 rains while non micronised DDT which would pass a 200-mesh screen was rendered ineffective by three periods of rain. It also depended to some extent on the vehicle as solid solutions in calcium stearate and stearic acid gave the best results a mortality above 80 per cent. being obtained after 86 days with 44 artificial rains. Mixtures with talc were effective for 30 days with 16 rains and those with stearic acid for 38 days with 20 rains.

Laboratory trials were also made of oil solutions applied as a film when 0.05 to 0.1 lb per acre were effective and of emulsions and suspensions with which 0.01 p.p.m. were effective for 8 to 10 days.



Field trials with dusts showed that 0.05 to 0.1 lb. per acre gave 100 per cent. kill but had no residual action. To secure this residual effect 1 to 2 lb. per acre had to be applied usually in the form of a 20 per cent. mixture with the vehicle. The duration of the effect varied with the type of water being longest (up to 8 or 10 weeks) where thick surface vegetation prevented the dusts from being blown to one side and least in the presence of sparse vegetation where application was again necessary two weeks after the first dusting.

Solutions in petroleum oils were less satisfactory than dust mixtures and, mainly owing to the difficulty of getting good coverage of the area with the oil film the effective dose was 0.1 lb. per acre and the resulting kill varied from 75 to 100 per cent. being usually over 90 per cent.

Two types of suspension were used in one DDT was in colloidal solution in the water and in the other it was in solution in xylene which was itself dispersed in colloidal-sized droplets. They showed very high promise and gave 94 to 100 per cent. kill which remained apparent for as long as three months. It is noted, however, that at high concentrations these suspensions were toxic to cold blooded animal life and killed fish, frogs and snakes as well as aquatic insects.

Large field trials were made with the object of controlling *Psorophora* mosquitoes the adult females of which lay their eggs in places liable to flood. Hatching of the egg occurs when the area is flooded and is followed by a very short aquatic stage. Two techniques were tried, in the one the soil liable to flood and containing eggs was treated, in the other surface applications were made to the water after the flood had occurred. In the first technique the application of DDT as a dust was ineffective but the application of solutions and emulsions at the rate of 0.1 lb. per acre at the first flood gave perfect results. Experiments were also made with a self-operating dispenser which released DDT solution automatically when the flood happened and this also was found effective.

Surface applications of 0.1 lb. DDT per acre by dusting, pouring of oil, spraying of oil or xylene emulsions or by using impregnated sawdust gave control, and in this case there was some indication of a residual action at the second time of flooding.

G Macdonald

METCALF R. L. HESS A. D. SMITH G. E. JEFFERY G. M. & LUDWIG G. W.  
Observations on the Use of DDT for the Control of *Anopheles quadrimaculatus*. *Pub Health Rep* Wash. 1945 July 6 v. 60 No. 27 753-74 1 text fig. & 4 figs. on 4 pls.

The median lethal doses of DDT and pyrethrins to laboratory reared *Anopheles quadrimaculatus* as shown by tests in a Peet Grady chamber are —

	LD <sub>50</sub> in milligrammes per 1 000 cu. ft.	
	Males	Females
DDT	7.0	12.0
Pyrethrins	1.0	1.5

When tested as a residual insecticide doses of 40, 200 and 1 000 mgm. per sq. ft. showed no significant differences in initial toxicity the percentage mortality being determined by the period of contact of the mosquito with the treated surface which suggests that some physiological reaction such as the rate of absorption, limits its action. Surfaces treated with heavy doses retain

their toxicity however for a longer period than do those which have received smaller doses a fact which was confirmed in laboratory and field tests. In the former a 60-minute contact of female *A. quadrimaculatus* with films of different strengths and ages produced the mortalities shown below —

Age of Film	Dose of DDT in milligrammes per square foot		
	40	200	1 000
	Per cent	Per cent.	Per cent.
New	100	100	100
1 week	100	100	100
2 weeks	100	100	100
4 weeks	100	100	100
8 weeks	20	71	100
12 weeks	44	62	100
16 weeks	0	22	30

Males were more readily killed than females and shorter periods of contact showed the same general effect of ageing of films. In field experiments the toxicity of films of 20 mgm per sq ft dropped below a useful level after about 18 weeks and this loss of toxicity appeared to be mainly due to crystals flaking off the surface rather than to volatilization. Vibration as in ordinary occupation of a house accelerates this effect.

Practical trials were made of an emulsion consisting of a 1 in 4 dilution of a stock concentrate of 25 per cent DDT 7 per cent Triton (emulsifier) and 68 per cent xylene applied by means of a portable hand spray with which two men could treat about 20 houses per day. Direct measurement of the efficacy was made difficult by the small numbers of mosquitoes in control houses but liberation of adult mosquitoes into the houses showed that the films remained effective for the remainder of the season the period required for complete knockdown in an inhabited house 8 weeks after treatment being 230 minutes. It was noted that smooth enamelled or smooth papered surfaces lost their toxicity more rapidly than rough wallboard.

Both in houses and experimental kegs left in the open it was noted that those treated with DDT exerted a definite repellent effect and in newly treated houses there was a marked decrease in the biting rate despite the entry of mosquitoes an effect which decreased however with the ageing of the films. It appeared that DDT does not deter mosquitoes from entering a treated room but exerts an irritant effect after they have been in contact with a treated surface for a short time. However at least 95 per cent and probably almost 100 per cent. receive a lethal dose before leaving houses and the chain of malaria transmission is thereby effectively broken.

Emulsions of DDT solutions in kerosene were effective larvicides when the dose of DDT amounted to 0.1 lb per acre of water surface. Some difficulty was met in applying powdered DDT from aircraft owing to caking of the substance when its concentration in inert dust exceeded 5 per cent. With dust dilutions of this nature 90 per cent. larval control was obtained over 200 foot swaths at actual application rates as low as 0.05 lb per acre but this involved carrying a heavy load of inert dust and thereby counterbalanced any advantages gained by applying DDT in this form. The spraying of kerosene solutions from aircraft also presented some technical difficulties and an unduly high payload so that the authors turned to 15 to 40 per cent solutions of DDT in certain polymethylnaphthalenes which when sprayed from a specially developed apparatus on a Stearman plane gave 90 per cent or better

kills over a swath 200 to 300 feet wide at doses of DDT of less than 0.03 lb. per acre. Considerable trouble was spent on the development of thermal generators DDT solution being discharged into an extension of the exhaust and an apparatus was finally devised which produced a visible aerosol, 80 per cent. of the droplets in which were between 5 and 100 microns in diameter this was satisfactory and gave 80 per cent. larval kills over a swath 300 feet wide at application rates of 0.04 lb. per acre. It was also very effective in killing adult mosquitoes, both caged and wild even when protected by dense woods though for this purpose a dose of 0.4 lb. per acre was needed. Aerosols of this nature were much superior for this last purpose both to smokes with finer droplets and to coarser sprays. Another advantage of this type of application was that it was much less toxic to other aquatic insects than the application of kerosene solutions.

G Macdonald

SIMMONS, S. W. & Staff. Tests of the Effectiveness of DDT in *Anopheles* Control. Pub Health Rep Wash. 1945 Aug 10 v. 60 No 32, 917-27 3 figs.

The value of DDT as a residual spray has been tested in a series of field and laboratory experiments the scale of which can be estimated from the fact that 33 000 adult *Anopheles quadrimaculatus* have been used in 1,800 individual tests and the main results of which are well illustrated in graphs showing the rate of knock-down of mosquitoes exposed to films of different ages the comparative values of various solutions and emulsions and the comparative pattern of various doses of DDT. The first follows the now generally accepted vehicle was a Lethane water emulsion which gives an amorphous deposit probably covered by a protective film of the solvent. The most satisfactory emulsion was a 35 per cent. solution of DDT in a light proprietary oil known as PD544 C emulsified in water with 4 per cent. Triton (100) in xylene as PD544 C or 0.5 per cent. "Arctic Syntex A" as emulsifying agents. Emulsions in which the dispersed phase was cyclohexane or cyclohexanone were slightly less effective and about equal to kerosene solutions. [It would appear though not certainly that these tests were carried out on unpainted wood panels. Other recent work suggests that kerosene solutions are much less effective against flies on painted surfaces.] An interesting note is made may throw some light on this varying effect. Kerosene solutions leave long fragile needle-shaped crystals. Crystals from emulsions are on the whole smaller in some cases less fragile and more compact while Thanite and Lethane leave amorphous deposits which may be covered by a protecting film of the solvent.

The effect of varying the dosage of DDT is to vary the minimum period of contact needed to secure 100 per cent. mortality but as a practical point it seems that films ten weeks old, varying from 50 to 300 mgm. per sq. ft. give about the same mortality amongst mosquitoes exposed to them for 60 minutes though after the ten-week observation period the 50 mgm. dose may lose toxicity earlier than the 100 mgm. dose.

The overall cost of treating the average tenant house (1 700 sq. ft. of wall and ceiling surface) with a DDT xylene Triton-water emulsion at a dose of 200 mgm. per sq. ft. varied from \$1.50 to \$1.75 and this low cost is considered to prestage a degree of malaria control not previously obtainable. A series of releases of 800 to 2,000 mosquitoes in treated rooms showed that this dose was still effecting a complete kill after 22 weeks.

When applied at a dose of 0.1 lb per acre either in surface films emulsions or suspensions DDT will kill all anopheline larvae within 24 hours. The technique used was to prepare emulsions or other vehicles of such a strength that a total quantity of 15 to 20 gallons per acre gave the required dose of 0.1 lb and considerable saving was thus achieved in material costs compared with oil [but not in labour costs]. In making surface films an emulsion of DDT/oil solution was made in water using an emulsifying-spreading agent [1.25 per cent DDT 0.5 per cent B-1956 (an emulsifying-spreading agent) in No. 2 fuel oil of which one gallon is mixed with 15 to 20 gallons water]. A type formula for emulsions was DDT 35 per cent in xylene with Triton X 100.

Duponol OS or comparable emulsifiers and suspensions were prepared by dissolving the DDT in a water miscible solvent such as alcohol and adding to water with a dispersing agent.

From 90 to 95 per cent of the kill takes place within the first hour after treatment and the residual effect wears off within a few days though the sub-surface water when abstracted and tested in the laboratory remains toxic to larvae for a rather longer period. DDT has virtually no effect on plankton and some larger forms of life such as *Daphnia*. When the dose is considered not in relation to the water surface but in relation to its volume quantities between 0.02 and 0.2 parts per million have very similar effects.

The ultimate destruction of the DDT seems to be the result of action by the bottom mud complex as laboratory trials show that destruction takes place much more rapidly in its presence than in its absence.

G Macdonald

## TRYPANOSOMIASIS

**HARDING R. D.** Late Results of Treatment of Sleeping Sickness in Sierra Leone by Antrypol, Tryparsamide, Pentamidine, and Propamidine, Singly and in various Combinations. *Trans Roy Soc Trop Med & Hyg* 1945 Oct v 39 No 2 99-124

This is an account of the effects of treatment followed for 13 to 28 months (in a few instances up to 46 months) in 2713 cases of sleeping sickness in the Kailahun District of Sierra Leone. A report on the earlier results of treatment in a large proportion of these cases has already been published [this *Bulletin* 1943 v 40 370]. Deaths since the start of treatment totalled 228 (of which 181 were attributed to sleeping sickness or the toxic effects of the drugs employed) and only 126 cases remained untraced.

The courses of treatment employed were as follows —

- (i) Antrypol five doses of 1 gm. at 5-day intervals in cases with a normal cerebrospinal fluid cell count.
- (ii) Tryparsamide six to ten doses of 2 gm. at 5-day intervals. The majority of patients received nine or ten doses.
- (iii) Antrypol, three doses of 1 gm. followed by tryparsamide three to five doses of 2 gm. all at 5-day intervals.
- (iv) Three other combinations of antrypol and tryparsamide designed to reduce the toxicity exhibited by Course iii —
  - (a) Antrypol, three doses of 1 gm. followed by tryparsamide three to seven doses of 2 gm. An interval of 5 or 7 weeks separated the first and second doses the remainder being given at 5-day intervals.
  - (b) Antrypol, two doses of 1 gm. followed by tryparsamide four to six doses of 2 gm. at 5-day intervals.
  - (c) Antrypol one dose of 1 gm. followed by tryparsamide eight or nine doses of 2 gm. at 5-day intervals.
- (v) Pentamidine eight to twelve doses of 50 to 100 mgm daily.
- (vi) Propamidine, eight doses of 50 to 75 mgm. daily.

The remaining three courses constituted a small-scale trial of a combination of pentamidine and trypanamide administered concurrently —

- (vi) Pentamidine five doses of 100 mgm. and trypanamide, five doses of 2 gm., at 5-day intervals. On each treatment-day both drugs were given, the pentamidine first, and trypanamide about two hours later.
- (vii) Pentamidine, five doses of 100 mgm. daily and trypanamide five doses of 2 gm. at 5-day intervals. Trypanamide was given on the first treatment day, pentamidine on the 2nd to 6th days inclusive and trypanamide again on the 7th, 12th, 17th and 22nd days.
- (ix) Trypanamide alone five doses of 2 gm., at 5-day intervals, to serve as a control for Courses vi and vii.

Cerebrospinal fluid cell-counts had been made before treatment in 1170 cases in 579 of whom this examination was repeated usually together with an estimation of total protein, at the final follow-up. Cerebrospinal fluid was also examined, at the final follow-up in 383 other patients in whom lumbar puncture had not been performed at the start of treatment.

The author discusses the relative importance of various criteria in assessing the results of treatment —

- (i) *Clinical condition* — This is regarded as unreliable since some patients with considerably raised C.S.F. cell-counts may appear quite well, whilst others with normal counts may present symptoms which superficially suggest relapse but which are really attributable to other causes.
- (ii) *Presence or absence of trypanosomes* — This is valueless, since trypanosomes were only found in four instances (two in gland juice, one in blood, and one in C.S.F.) in 1732 cases re-examined subsequent to treatment, and the true incidence of treatment failures is certainly higher than suggested by these figures.
- (iii) *C.S.F. picture* — This is considered the only reliable criterion of cure in survivors, though it may perhaps be complicated by the co-existence of yaws in a community since this disease apparently may rarely give rise to slight abnormality of the cerebrospinal fluid (this *Bulletin* 1936, v 33, 863; 1940, v 37, 25; 1942, 39, 46). However yaws probably invalidates the criterion only to a very slight extent in 20 random individuals who had no history of sleeping sickness, and an unknown history in regard to yaws (which affects considerably more than half the population of this district at some time of their lives, generally in early childhood). Harding found that 19 showed 5 cells or less and one showed 67 cells per cmm. of C.S.F.

A cell-count was considered to be a more sensitive index of the results of treatment than a total protein estimation. Thus, in 917 fluids examined for cells and protein, at the final survey 71 were abnormal in that they showed cells above 10 or protein above 35 mgm., or both these features, but only 7 of the cases showed protein above 35 mgm. combined with a cell-count of 10 or less. The omission of protein estimation would, therefore, have entailed an error of about 10 per cent in recording abnormal fluids, but in calculating total numbers of cases in which treatment failed, including those patients who died or became blind, the error would be no more than about 2 per cent.

In a minority of cases the cell-count was found to remain slightly raised up to three or four years after treatment even though there seemed every indication that the patient was cured. For this reason the author adopts 10 cells per cmm. as the limit of normality in assessing the cure-rate, but in order to satisfy the most stringent standards he has also worked out cure rates on the basis that five cells per cmm. represents the upper limit of normality after cure. A definite decision as to cure cannot be reached within about 15 months after treatment.

- (iv) *Mortality* — A history of death from sleeping sickness is, of course, of prime significance in assessing the results of treatment so long as the accounts of relatives and friends can be relied upon, as was found generally to be the case among the people concerned.

The author treats his findings by statistical methods designed to show the comparative value of the various forms of drug therapy in the mass treatment of a sleeping sickness outbreak which exhibits the distribution of evolutionary stages of the disease (as revealed by C.S.T. cell-counts) encountered in this particular epidemic. The distribution as percentages of all cases of sleeping sickness in which lumbar puncture was done before treatment was as follows: 0-5 cells per cmm. 52.2 per cent 6-20 cells 26.1 per cent 21-100 cells 9.1 per cent. more than 100 cells 12.5 per cent. The statistical methods used are fully described and are similar in principle to those generally employed in calculating standardized death rates from crude death rates.

Course II comprising three doses of antrypol followed by three to five doses of tryparsamide all at 5-day intervals proved to be highly toxic being followed by a standardized death rate of 6.4 per cent within three months of treatment. However the toxicity and death rates associated with this course were considerably reduced by the adoption of course IV where there was an interval of five to seven weeks after the first dose of antrypol or where only one or two doses of antrypol preceded the administration of tryparsamide. In fact this course (IV) proved to be the most successful of all with a standardized cure rate of 93.5 per cent. Attempts to determine the underlying reasons for the exceptional toxicity of Course III were unsuccessful and the author considers that the most likely explanation of the great reduction in toxicity when the course was modified by merely allowing an interval of five to seven weeks between the first two antrypol doses is that the long interval allowed time for recovery in the patients' general condition after the initial dose had destroyed all trypanosomes in the peripheral circulation.

Course II (tryparsamide alone) was rated inferior to course IV largely because of the high incidence of blindness—5.6 per cent though the figure is somewhat weighted by the high proportion of late cases treated and vision is more frequently impaired in these than in early cases. Courses V and VI (diamidines) were inferior because of their failure to cure late cases.

A satisfactory rule for all occasions was eventually worked out if it is convenient to arrange an interval of 3 weeks or more without treatment after the first dose of antrypol has been injected then a further two of antrypol followed by five of tryparsamide are given. If the interval is between 2 and 3 weeks only one further antrypol and six tryparsamide are given and if the interval is less than 2 weeks then no further antrypol is administered and the course is completed with seven doses of tryparsamide. This rule has since been applied over many thousands of cases and it has been consistently found that no more than about 1 per cent of patients die during treatment and no more than 1 per cent become blind.

An important part of the paper deals with the value of combined treatment by antrypol or pentamidine and tryparsamide. The author writes that it is generally less upsetting to the African peasant's farm work and normal life to visit a treatment centre once every 5 or 7 days than to visit it daily for the same number of times whereas such a patient would not be willing to make a journey of more than 3 or 4 miles daily for perhaps 10 days he will and does walk four times that distance regularly once in 5 days on ten occasions. Greater practical advantage would therefore accrue from reducing the number of attendances necessary in the spaced type of course while retaining its effectiveness than from reducing the intervals between injections. Such an aim might be realized by employing a combination of tryparsamide with another drug such that the two compounds could be administered concurrently in full doses without undue toxicity. Antrypol as the second drug does not meet the need because when given concurrently with tryparsamide the dose of one or both drugs must be substantially reduced for the combination to be

tolerated. Pentamidine however was safely given in full doses of 100 mgm. combined with five full doses (2 gm.) of tryparsamide both drugs being given on each of five injection days at 5-day intervals, so that the whole course was completed in the short span of 3 weeks. The small-scale trials of combined pentamidine and tryparsamide (Courses vii to ix) involving 84 cases appeared to give very promising results but it was not possible to claim any superiority of the combination over tryparsamide alone since the average Sierra Leone patient is so readily cured by tryparsamide without any adjuvant. The risk of toxic sequelae and visual impairment with the pentamidine tryparsamide combination appears to be very slight and the author recommends it for more extended trial in other parts of West Africa, where the average case is less responsive to treatment with tryparsamide.

The author has also studied the protection against subsequent reinfection conferred by treatment. In 1732 cases comprising 1610 probable cures and 122 relapses re-examined at the final follow-up trypanosomes were found in only four cases, although at least 41 reinfections might have been expected among the cured cases on the basis of the prevailing infection rate of the general population in the interim between mass-treatment and follow-up. Of these four cases three had been treated by tryparsamide alone and probably were in fact reinfected individuals because they had large soft glands suggestive of recent infection, and an almost normal C.S.F. picture. The fourth patient who had received antrypol was probably suffering a relapse, being clinically far advanced and with a high C.S.F. cell-count. In summary then no reinfections were demonstrated in 1,807 cases treated by courses containing antrypol or a diamidine though 33 might have been expected, whilst three reinfections occurred among 300 cases treated by tryparsamide alone when eight might have been expected. The tentative interpretation offered is that all the treatment-courses produced a temporary immunity due to the destruction of trypanosomes while antrypol and the diamidines (but not tryparsamide) exerted in addition a prophylactic action persisting for over a year. Harding writes that these findings are not necessarily representative of results which would be obtained in all parts of West Africa and much depends no doubt on the local strain of trypanosome. In one small area in Nigeria, for example, he found trypanosomes in a large proportion of cases of relapse after treatment by tryparsamide alone but in general his experience has been that trypanosomes are rarely to be found in relapses after combinations containing antrypol. Nevertheless in another part of Sierra Leone where an unusual type of the disease prevails about 9 per cent. of a group of cases revealed trypanosomes 18 months after treatment with a combination of antrypol and tryparsamide but whether they represented relapses or reinfections was not determined. Taking all such variations into account, the author's view is that it probably remains true that in most types of West African trypanosomiasis, the inclusion of antrypol, or of a diamidine in treatment courses reduces the danger to the community arising from the possibility of subsequent infectious relapse or reinfection among the cases treated.

E. M. Louie

DIAS E. & DE FREITAS L. Jr. Introdução ao estudo biométrico dos hemoflagelados do género *Schizotrypanum*. I. Introdução material e técnica problema e métodos estatísticos. [Introduction to a Biometrical Study of Haemoflagellates of the Genus *Schizotrypanum*. I. Introduction, Material and Technique, the Problem and Statistical Methods.] *Mém Inst Oswaldo Cruz*. 1943, June 1, 38 No. 3 427-36 1 fig. [14 refs.]

This is the first instalment of a series of papers devoted to a biometrical study of *Trypanosoma cruzi*-like haemoflagellates which the authors refer to

the genus *Schizotrypanum*. This group comprises trypanosomes parasitic in various species of mammals and especially bats in different parts of the world. Since these trypanosomes are morphologically similar to the parasite of Chagas's disease it is important both from the aetiological and epidemiological points of view to determine whether they represent one species or a number of distinct species.

In the present paper the authors describe the methods employed for the differentiation of various strains of trypanosomes measured in blood films stained by one of the Romanowsky methods. In each strain 50 trypanosomes are drawn with the aid of a camera lucida at a magnification of 1500. The measurements are then made with an opisometer along a line running through the middle of the body of the trypanosome from the posterior end to the tip of the flagellum. They comprise the following elements: (1) Distance from posterior end to middle of the nucleus (PN) (2) distance from middle of the nucleus to anterior end of the body (NA) (3) length of free flagellum (F1) (4) total length (T) (5) nuclear index (IN) representing  $PN/NA$ .

The statistical problem was to determine whether the strains thus measured belonged to the same or to different populations. The authors consider that from this point of view the most important elements are NA and the mean nuclear index (INM) which is the mean of the individual nuclear indices (IN) of a strain. The strains are compared with each other by calculating the arithmetic mean of each series of measurements and the standard errors of the differences between the means and also by applying Pearson's  $\chi^2$  test.

C. A. Hoare

DIAS E & TORREALBA J. F. Verificação de flagelados semelhantes ao *Trypanosoma rangeli* Tejera em *Rhodnius prolixus* alimentados em caso de doença de Chagas na Venezuela. Considerações sobre a natureza deste protozoário. [Flagellates similar to *Trypanosoma rangeli* in *Rhodnius prolixus* fed on a Case of Chagas's Disease in Venezuela. Discussion of the Nature of this Protozoon.] *Mem Inst Oswaldo Cruz* 1943 Dec. v 39 No 3 265-78 35 figs on 2 pls [12 refs.] English summary.

In 1920 TEJERA [see this Bulletin 1921 v 17 97] described under the name *Trypanosoma* (or *Crithidia*) *rangeli* a flagellate represented chiefly by crithidial forms which he found in the gut of *Rhodnius prolixus* from Venezuela. In some of the bugs this parasite occurred alone in others it was accompanied by metacyclic forms of *T. cruzi*. Tejera suggested that this parasite might also have some vertebrate host.

In the present paper the authors claim to have isolated *T. rangeli* from man. The case in question was in a child in Venezuela who showed symptoms of acute Chagas's disease. The patient's blood was inoculated into a guinea-pig and laboratory-bred *Rhodnius prolixus* were fed on the patient for xenodiagnostic purposes. The bugs thus fed became infected with flagellates which comprised crithidial forms similar to *T. rangeli* and metacyclic trypanosomes while in the blood of the guinea-pig were found trypanosomes of the genus *Schizotrypanum* to which the authors refer *T. cruzi* and some closely related bat trypanosomes. The trypanosome in question was differentiated from *T. cruzi* biometrically its closest affinities being with *T. phyllostomae* a bat trypanosome previously suspected of being capable of infecting man. The same trypanosome was also seen in a monkey inoculated from infected bugs and in guinea-pigs through which the strain had been passaged. However the flagellates which developed in Triatomid bugs fed on these animals did not belong to the *rangeli* type but were of the *cruzi* type.



In discussing the nature of the new trypanosome the authors dismiss both the possibility of a mixed infection (*T cruzi* and *T rangeli*) in the bugs since these insects had been bred in the laboratory and the possibility of it being an atypical strain of *T cruzi*. They attribute all the stages seen in the bugs and in the mammals to *T rangeli* which they regard as a pathogenic human trypanosome.

[There are a number of conflicting facts in this paper which stand in need of further elucidation before the authors' conclusions can be accepted. (1) It is admitted that the symptoms in the patient from whom "*T rangeli*" was isolated were those of typical Chagas's disease as produced by *T cruzi*. (2) The blood-form of *T rangeli* has the general appearance of *T cruzi* from which it differs only in its mean nuclear index" (see DIAS & FREITAS, above) and mean total length. In other words there is evidently considerable overlapping in the dimensions of the two trypanosomes which would hardly justify their separation into distinct species especially as no information is given regarding the degree of variation in undoubted strains of *T cruzi*. (3) It would appear that while the crithidia in the bugs infected from the patient correspond to Tejera's *T rangeli* in having a small kinetoplast both the blood form of the new trypanosome and its metacyclic form in the bug have a large kinetoplast like that in *T cruzi*. Since the kinetoplast of a given trypanosome retains its characteristic size throughout the entire cycle of development in vertebrate and invertebrate hosts the discrepancy found in the present case (but not commented upon by the authors themselves) is rather suggestive of a mixed infection of *T cruzi* and Tejera's flagellate. (4) The problem is further complicated by the fact that *rangeli*-like crithidia developed only in the bugs which had fed on the patient, but not in those which were subsequently fed on experimentally infected animals.]

C. A. Hoare

ROMAÑA, C. & TERRACINI, E. Infección de lauchas por *S. cruzi* a través de la piel intacta. [Infection of Mice via the Intact Skin.] *An. Inst. de Med. Regional Tucumán*. 1945 Aug. v. 1 No. 2, 135-40. [10 refs.] English summary.

"(a) The authors have obtained with *S. cruzi* the infection of mice through the apparently intact skin.

(b) The prepatent period lasted 73 days in the infected animals.

(c) The infection showed a chronic character from the beginning.

ROMAÑA, C. & TERRACINI, E. Comportamiento de las infecciones de lauchas por *S. cruzi* según la concentración de parásitos inoculados. (Infecciones crónicas iniciales.) [The Course of Infections of Mice with *T. cruzi* according to the Number of Parasites Injected.] *An. Inst. de Med. Regional Tucumán*. 1945 Aug. v. 1 No. 2, 141-64. 5 graphs. English summary.

LARCHER, M. & ROMAÑA, C. La puerta de entrada cutánea en los casos humanos de enfermedad de Chagas. [The Portal of Entry in Human Cases of Chagas's Disease.] *An. Inst. de Med. Regional Tucumán*. 1945 Aug. v. 1 No. 2, 165-75. 3 figs. [12 refs.] English summary.

The local swelling associated with the bite of the vector of *T. cruzi* has often been described but the authors here give a detailed account of the lesion. It is red, oedematous, hard and slightly painful on palpation. The associated glands, preauricular and submaxillary are tender and if sections of the former are examined, developmental forms of *T. cruzi* are seen, and soon general symptoms appear and trypanosomes are present in the blood. In some cases

the site of the bite is like a furuncle or an anthrax pustule of mild intensity. In others there is superficial rather than deep extension and an erysipelatoid condition is produced. It then gradually clears up the skin becomes dry and undergoes a furfuraceous desquamation leaving a small nodule or a pigmented spot.

A case in point is detailed. A man of 27 years the primary lesion was at first thought to be pyogenic and he was treated with sulphonamides but without benefit. He also had a rose rash on the chest and shoulder slightly raised disappearing on pressure. The primary lesion of the eyelids and face were erysipelatoid next day and then began to clear up. A fortnight after admission the patient complained of pain in the bones especially the long bones. Complement fixation was now weakly positive. In another fortnight the reaction was definitely positive and after another 14 days strongly so. The local lesion gradually disappeared and two months after admission to hospital the only indication of it was a slight pigmentation of the skin.

H. Harold Scott

ROMANA C. Parasitismo por *S. cruzi* de válvulas de corazón de perro [Infection of the Cardiac Valves of the Dog with *T. cruzi*] *An. Inst. de Med. Regional Tucumán*, 1945 Aug. v. 1 No. 2 207-11 2 figs. English summary.

The author refers to the finding in the atrio-ventricular valves of a dog's heart of focus of multiplication of *S. cruzi* describing the local histopathological reaction produced by the parasite.

ENGEL R. Tumorstwachstum und Chagaskrankheit [New Growths and Chagas's Disease] *Klin. Woch.* 1944 Mar/Apr. v. 23 Nos. 9/10 127-9 3 charts [11 refs.]

ROSKIN and ROMANOWA have reported the cure of experimental cancer by means of the toxin of *T. cruzi* but says the author the story of the treatment of cancer is loaded with uncritical communications and defective experiment. Next Rudolf SCHMIDT as long ago as 1910 decided that he was convinced by statistical figures that those who had recovered from several infective diseases were less liable to malignant disease than those with a low infective index.

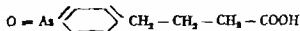
ROSKIN and ROMANOWA (*Acta Cancerol.* 1935 v. 1 323) noted that in Chagas's disease after the acute stage subsides the trypanosomes disappear from the blood and collect in leishmania form in the heart, brain and internal organs and when present in tumour cells. Next if tumour emulsion and *T. cruzi* are inoculated together the latter infection gains the ascendancy the tumour dwindles and may even disappear altogether. They went a step further and prepared a toxin of the trypanosome from centrifuged citrated blood cooling it and again heating to destroy the trypanosomes themselves, and they claimed that increasing doses of this endotoxin-containing material first retarded and then prevented the growth of the tumour without harming other tissues or organs.

The author has carried out experiments with large numbers of mice which are very susceptible to *T. cruzi* infection the tumour being one to which mice are liable (mouse ascites tumour). These experiments were carefully performed, but the author was unable to confirm the work or report of Roskin and Romanowa. The toxin in the acute stage had no beneficial effect on the tumour growth and the tumour was absolutely unaffected in its course by Chagas's disease in its chronic stage or after cure. So much for the mouse tumour the application to cancer in human beings has not yet been tested (but one gathers from the general tone of the paper that success would come as a surprise).

H. Harold Scott

TALICE, R. V. & LÓPEZ FERNÁNDEZ, J. Primeros ensayos de tratamiento de las formas agudas de enfermedad de Chagas con un nuevo arsenical (ácido *p*-arsenofenilbutírico) [Trial of a New Arsenical in the Treatment of Acute Chagas's Disease.] *Arch. Uruguayas de Med. Ciruj. y Especialidades*. 1945 July v 27 No 1 33-46, 3 charts. English summary

The best treatment hitherto known for acute cases of Chagas's disease has been Ac. 7602, a German preparation which of late has not been obtainable. The preparation here referred to is *p*-arsenophenyl butyric acid, with the formula



It has been found of service a year ago for African trypanosomiasis by EAGLE the protozoon disappearing from the blood within an hour of the first injection.

For cases of American trypanosomiasis it has been used in a 2 per cent. solution in distilled water injected intravenously or intramuscularly three times a week in doses of 0.015 cc. per kilo body weight till 12 doses have been given. Three cases are recorded in this paper—two children, of 5 and 12 years respectively and an adult of 28 years. All three were clinically typical cases. The children tolerated the drug well—the adult had albuminuria after the second injection which necessitated reduction of the dose and longer spacing between injections (but no details are given of this reduction or lengthening of interval). The results noted are not too optimistic—the fever dropped in four days but other symptoms persisted, though the regional adenopathy was reduced. Xenodiagnosis positive before treatment was started, became negative after four days, but in the two children was again positive when they left hospital after the 12th injection. In untreated cases even when the form of disease is mild, the trypanosomes persist for a month at least. The clinical evolution of the disease seems to be uninfluenced. The fact that in the children the xenodiagnosis was negative for short periods only—7 and 12 days respectively—while it remained so in the adult, leads to the observation that larger doses should be given to children suffering from this disease.

H. Harold Scott

TALICE, R. V. Ensayo de tratamiento de la forma aguda de la enfermedad de Chagas por la penicilina. [Treatment of Acute Chagas's Disease with Penicillin.] *Arch. Uruguayas de Med. Ciruj. y Especialidades*. 1945 Aug., v 27 No. 2, 152-7 (1 chart & 4 figs). English summary.

One acute case of Chagas disease, in a 11 years boy has been treated with penicillin intravenously. The total doses reached to one million Oxford units which were distributed through 12 days of treatment.

The treatment had no beneficial action either from a clinical or a parasitological standpoint. The patient left the hospital still with a mild, slight fever and 12 xenodiagnoses carried on every day were all positive.

"Although only one case has been treated, we think that penicillin has no action over *Trypanosoma cruzi* infections. This result confirms our own experiments on laboratory animals."

PÉREZ, A. & ROMANA, C. Estado actual de antiguos casos de enfermedad de Chagas en una familia de Monteros (Tucumán) [The Present Condition of Patients with Long-standing Chagas's Disease in a Family] *An. Inst. de Med. Regional Tucumán*. 1945 Aug. v 1 No. 2, 213-28 6 figs. English summary.

Within the same family the authors establish the existence of —

"(a) An old acute case of Chagas disease—the first described in Argentina, 20 years ago now seemingly a simple carrier of *S. cruzi*

(b) An old case of Chagas disease with an apparent *spontaneous cure* examined 15 years afterwards. The isolated strains in both cases during the acute period showed little virulence.

(c) Finally the father had a myocardiac lesion probably caused by Chagas disease.

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### LEISHMANIASIS

GAST GALVIS A & RENGIFO S. Leishmaniosis visceral. Estudio epidemiológico del primer caso diagnosticado en Colombia. [First Case of Kala Azar diagnosed in Colombia.] Reprinted from *An Soc Biol Bogotá* 1944 Sept v 1 No 4 8 pp 3 figs.

During the course of a viscerotomy survey being carried out in Colombia in order to identify deaths from yellow fever sections of the liver from a child three years of age were found to contain numerous leishmania. The case was evidently one of kala azar the first to be identified in this country. A careful study of the inhabitants of the district San Vicente de Chucurí Department of Santander failed to reveal any other case. There was a 9.33 per cent incidence of malaria, a fact which renders difficult the recognition of cases of kala azar. During the survey which was carried out a number of cases of cutaneous leishmaniasis were seen. A study of the arthropods of the district showed that 15 species of *Phlebotomus* were represented. C M Wenyon

DA CUNHA A M. A soro-aglutinação das leishmanias [Serum Agglutination of the Leishmanias.] *Mem Inst Oswaldo Cruz* 1942 v 37 No 1 35-76 English summary

The author has investigated the possibility of identifying species of *Leishmania* by agglutination tests carried out with sera prepared by immunizing rabbits with culture forms of the organisms. The species employed were *L. tropica*, *L. infantum* and *L. donovani* of the Eastern Hemisphere and *L. brasiliensis* and *L. chagasi* (*L. donovani*) of the Western Hemisphere. A number of different strains of each species some of which had been in cultivation for years and others recently isolated, were used. Agglutination tests and absorption tests were carried out. The general results are given in a series of tables. It is concluded that all strains when freshly isolated have the same antigenic constitution. It was noted that when a serum which had been prepared against a freshly isolated strain is absorbed with an old strain the amount of agglutinin left free is much smaller than when a serum prepared against an old strain is absorbed with a newly isolated strain. It was shown that by absorbing equal amounts of serum prepared against a new strain by equal amounts by weight of a new and an old strain a newly isolated strain absorbs a larger amount of agglutinin than does an old strain. The absorbed sera were made to act on recently isolated as well as on old strains with the object of deciding whether the newly isolated strains contained a greater amount of the common antigen or whether they possessed a Vi antigen. The result indicated that the former view was correct. The antigen in newly isolated cultures is a common or primitive antigen which with increasing age of the culture is subject to modifications due to the production of secondary antigens which are not species-specific. The final conclusion is that species of *Leishmania* cannot be identified by serological agglutination tests. [Though this final conclusion may be correct as also the assumption that freshly isolated strains of all species contain a common antigen it is not clear that the recently

isolated strains contain no other antigen for the author has not applied the methods now generally employed for the antigenic analysis of bacteria and viruses e.g. exposure to the action of heat and various chemicals. The application of such tests might show that the results are capable of a different interpretation.] C M Wenyon.

SWENEY J S., FRIEDLANDER, R. D & QUINN F B. Kala-Azar (Visceral Leishmaniasis) simulating Splenic Anaemia. *J Amer Med Ass* 1945 Aug 4 v 128 No. 14 1020-22, 3 figs.

The case described is that of an Italian enlisted man 22 years of age who was admitted to hospital in Utah U.S.A. for an acute surgical condition of the abdomen. There had been a two-years history of illness which had commenced in Sicily. Numerous examinations failed to reveal the cause of the splenic enlargement and marked leucopenia which were features of the case. Finally the case was considered to be one of splenic anaemia. The spleen was removed, and a correct diagnosis was established by the discovery of leishmania in sections of the organ. Many previous examinations of preparations of the blood and bone marrow had failed to reveal the parasite. The patient was given a course of neostibosan and made an uneventful recovery.

C M Wenyon

ADLER, S., TCHERNOMORETZ I. & BER, M. The Action of some Aromatic Diamidines on Cultures of *Leishmania donovani*. *Ann Trop Med & Parasit* 1945 May 31 v 39 No. 1 14-19

The authors have tested a series of aromatic diamidines on cultures of *Leishmania donovani* with the object of correlating the results, if possible with those obtained in the treatment of experimentally infected hamsters as previously reported [this *Bulletin*, 1940 v 37 775 and 1942, v 39 748]. It was found that in the highest concentration of each drug which still permits survival and retention of motility of flagellates there is a definite inhibition and even abolition of the capacity to multiply. For each compound there is a fairly well defined maximum concentration which permits 90 to 100 per cent. of normal growth. There is no sharp end-point at which all the flagellates disappear. The two most effective drugs tested were 4-4'-diamidino diphenoxy propane [propamidine] and 4-4'-diamidino diphenoxy pentane [pentamidine] both of which have been shown to be inferior to 4-4'-diamidino stilbene [stilbamidine] in tests on hamsters. There is thus no correlation between the results of *in vitro* and *in vivo* tests though the four least effective compounds were in this position in both tests.

C M Wenyon

## FEVERS OF THE TYPHUS GROUP

SYLLA, A. Fleckfieberbeobachtungen. [Observations on Typhus Fever] *Deut Med Wochenschr* 1944 June v 9 No 8 263-72.

A clear and detailed description is given of the clinical features of typhus fever as observed by the author during the recent war. Numerous references are also made to papers already reviewed in this *Bulletin*.

Some points from the paper are as follows (the figures in brackets show the percentage incidence and when two figures are enclosed in one pair of brackets the first shows the incidence in cases with recovery the second refers to fatal cases).

The disease on the whole was mild the average fatality rate was about 6-7 per cent but there was a wide range of variation in different groups of cases the extremes ranged from 1 to 15 per cent Even during the same outbreak there might be great differences in severity at various stages of the epidemic. The incubation period ranged from 8 to 21 days. During the first three days the temperature fell to normal in some cases for a few hours then rose to about 39°C and persisted at that level The fever curve was usually of the continued type (89.3) but in some cases was remittent or intermittent A pseudo-crisis occurred in 12 per cent of the cases about the 10th day The termination was by lysis (70) or crisis (30) an after fever occurred in many cases (25.6)

The rash might be pale and scanty (50) dark red (38.7) or of irregular types such as papular scarlatiniform morbilliform etc. (4.5) petechiae were often seen (23 and 55) Pulmonary manifestations were bronchitis (50 and 65) bronchopneumonia (7 and 25.8) and lobar pneumonia (1.3 and 11) Cardio-vascular failure was attributed to myocarditis (10 and 49.7) or peripheral circulatory disturbance (13.8 and 86.5) Venous thrombosis was not common (1.6 and 3.7) gangrene was rare amputation of a limb was needed in only one case. Arterial spasm (1.3) rather than arterial thrombosis occurred in a few cases in the limbs.

The nervous manifestations were delirium (24.8 and 73.6) various psychoses especially mania and suicidal tendencies (6.3 and 34.9) tonic clonic spasms (1.1 and 24.8) nerve pareses (0.8 and 9.2) hardness of hearing (26) sometimes associated with inflammation of the middle ear (3.8)

Diagnostic importance was attached to the prolongation of the latent period of dermatophusm

Diarrhoea (17) enlargement of the liver (5) icterus (1.1) and enlargement of the spleen (58) were observed in the stated percentages. Slight albuminuria was usual the urine often contained red and white blood cells and cylindrical casts a true nephritis occurred in 10.8 per cent of the cases.

The blood picture was very varied leucocytosis occurred in about half of the cases leucopenia was not infrequent. The leucocytic index always showed a shift to the left Septic complications were few

The chief findings at autopsies were myocarditis slight (39.2) or severe (33) pneumonic complications (47) swelling of the kidneys (100) splenic enlargement (98) and oedema of the brain (100) No enthusiasm is shown for some of the special treatments that have been vaunted by some other German observers warm baths sulphonamides and atabrin were regarded as of doubtful value. Strophanthin caffeine and adrenaline were found useful glucose transfusions sometimes in concentrated form were occasionally needed. The general treatment was on orthodox lines.

*John W D Megaw*

CLAUS G. *Über Mittelohr und Warzenfortsatzentzündung bei Fleckfieber*  
[Middle-Ear and Mastoid Inflammation in Typhus Fever] *Deut Militärarzt*  
1944 Aug v 9 No 8 366-70 2 figs [12 refs.]

Four cases are described in which pyogenic complication affected the middle ear with extension to the mastoid process Although the condition is not common it is not so rare as is generally supposed and it deserves attention because of the danger of extension to the lateral sinus. Two exceptionally clear X ray photographs illustrate the paper and a description is given of the operative technique.

*John W D Megaw*

ROGNER, R. Physiologisch-chemische Untersuchungen bei Fleckfieberkranken. [Biochemical Investigations in Typhus.] *Dtsch. Monatsschr.* 1944 Aug., v 9 No 8 37-60 1 fig

An investigation of the non-protein nitrogen, sugar and chloride concentrations of the blood and blood serum in typhus fever

ROBERT, C. Notes sur le typhus exanthématique observé à Buchenwald. [Typhus in the Buchenwald Concentration Camp.] *Bull et Mém. Soc. Méd. Hôp. de Paris* 1943 Nos 15/16, 183-7

ECKE, W. Proteus-OV19-Agglutination und Rickettsien-Agglutination bei Fleckfieberimpfungsempfängern [Proteus OV19 and Rickettsia Agglutination Reactions in Persons Protected by Typhus Vaccines.] *Dtsch. Monatsschr.* 1944 Apr v 9 No. 4 188-91 [10 refs.]

The titres observed in groups of persons vaccinated (presumably recently except in the group vaccinated 4-6 months previously) with Weigl's loose vaccine or a Cox type vaccine were as shown in the table. With regard to the first group of 130 it is stated that 109 had received Weigl's vaccine and 21 the Cox type vaccine—positive reactions were relatively much more numerous in the latter sub-group but no details are given.

Well-Felix Titres

	Negative	1-50	1-100	1-200	1-400
Among 130 vaccinated	51	31	31	15	2
Among 49 vaccinated 4-6 months previously	34	7	4	4	0

Rickettsia-Agglutination Titres

	Neg	1-20	1-40	1-80	1-160	1-320	1-640	1-1,280
Among 100 vaccinated	2	3	8	41	19	12	12	1

John W D Meyer

SHOUKRI, Y. S. Bedside Typhus Diagnosis. *J Roy Egyptian Med Ass.* 1945 May v 28 No. 5 231-45.

The introductory "blurb" states that the method described is "A quick and simple variation of the Well-Felix reaction giving positive results much earlier than the original test in 50 per cent. of the cases."

The test is a slight variant of a well-known slide test. A droplet of finger blood is mixed with a drop of plain water—a drop of a thick suspension of *Proteus* O19 stained with methylene blue is added and stirred in for 30-60 seconds. The method of preparing the suspension is described. The growth from 10 agar 20-hours slope cultures is mixed with 10 cc. distilled water and two drops of formalin are added. After filtering the suspension through a thin layer of cotton, 0.2 cc. German Loeffler's blue solution is added—the mixture is well shaken and kept in the incubator for a day or two being shaken twice daily during the process. It is again filtered through cotton and another drop of formalin is added.

The degree of dilution of the blood on the slide is 1-7

It is claimed that the use of water and formalin abolishes the agglutination inhibitory zone of the serum that the water prevents coagulation and haemolyses the red corpuscles and that false positives due to natural agglutinins do not occur

From the table showing the results of comparative tests it appears that all titres below 1-125 with the standard Weil Felix test are shown as negative results This arbitrary elimination of weak positives must be taken into account in estimating the significance of the findings *John W D Megaw*

LORENTZ F H Der Trockenfolientest zur raschen Erkennung des Fleckfiebers  
[The Dry-Leaf Test for the Rapid Diagnosis of Typhus Fever] *Med Ztschr*  
1945 Jan. v 1 No 4 128-30 6 figs.

The author describes the results obtained in a large series of tests carried out by the method introduced by EYER and BRIX [see this *Bulletin* 1944 v 41 23] The only special requisite for the test is a supply of ready prepared slips of paper on each of which a drop of stained suspension of *Proteus OX19* has been dried but details of the technique will be of interest only to workers engaged in testing the various rapid modifications of the Weil Felix reaction.

From the present paper it is evident that the method demands a good deal of practice the first series of 100 tests yielded a number of anomalous results and so have been discarded from the final analysis which deals with a series of 1 000 consecutive tests and compares the findings with those obtained by means of the standard reaction

A general degree of agreement is claimed between the two tests and broadly speaking the relationship between the reactions was as follows Negative reactions correspond to negative Weil Felix responses weakly positive reactions ( $\pm$ ) correspond to titres of about 1-200 positive reactions (+) to titres of about 1-600 and the two highest grades of reaction (++) and (+++) to titres of 1-3 000 and over

The table shows that there was a good deal of variation from this standard for example among 106 negative reactions with the rapid test there were 52 in which the Weil-Felix titre was  $\pm$  1-100 or +1-100

Among 378 weakly positive reactions the Weil Felix titres were  $\pm$  1-100 in 73 +1-100 in 57 +1-200 in 176 +1-400 in 61 +1-800 in 9 +1-1600 in 2.  
*John W D Megaw*

CLAVERO G & GALLARDO F P Grounds Intradermic Test in Typhus Fever Infection Personal Observations, Techniques, and possible Applications *Bull Health Organisation* (League of Nations) 1943/44 v 10 No 4 700-2t 8 figs on 4 pls. [30 refs.]

The original article was reviewed in this *Bulletin* 1943 v 40 530

SCHMIDT W Erfahrungen zur Therapie des Fleckfiebers. [Experiences in the Therapy of Typhus Fever] *Deut Militärarz* 1944 June v 9 No 6 273-6 1 fig

The author claims to have saved a number of lives by injections of insulin—which in severe cases was given up to the point of causing hypoglycaemia—followed by the administration of glucose preferably by the mouth but intravenously when necessary The dosage of insulin when possible was based on blood sugar estimates during the fasting period. Comatose patients were given up to 20-30 gm glucose intravenously every day



The fatality rate in a group of patients treated by insulin and glucose when necessary was 6.3 per cent. In another group stated to be comparable in all other respects, the rate was 11.9 per cent., but no information is given with regard to the size of the two groups or the other circumstances which justified a statistical comparison of the results.

*John W. D. Meyer*

SCHONBRUNNER, E. Strophanthin und Digitalistherapie bei Fleckfieber [Strophanthin and Digitalis Therapy in Typhus Fever] *Dtsch. Med. Woch.* 1944 Sept., v. 9 No. 9 412-15 4 figs. [27 refs.]

Full details are given of an exceptionally severe case of typhus fever in which the pulse rate rose to 160 on the 14th day and continued to rise in spite of "strophanthin-glucose thrice daily." On the 16th day the rate was 170-190 and frequent doses of strophanthin were given intravenously amounting in all to 1.25 mgm. The rate rapidly fell to 100 and there was a great improvement in the patient's condition.

The strophanthin-effect lasted a short time and in spite of further injections the rate rose as high as before. Digitalis was given in the form of 2 cc. "Digipur" every six hours and the rate fell promptly to 100-140. By the 26th day the improvement was so great that the dose of digitalis was given only once daily.

The author states that there are practically no contraindications to the "strophanthin (digitalis) treatment in typhus fever whether the circulatory failure is due to myocarditis or to damage to the vasomotor centres.

In the case described the reductions in the pulse rate were due to the production of a 2-1 heart block, as is shown by the electrocardiograms.

*John W. D. Meyer*

GRUBEL, W. Ueber die Fleckfieber Rekonvaleszenz mit besonderer Berücksichtigung des Kreislaufes [Convalescence in Typhus Fever with special reference to the Circulatory System.] *Monat. Med. Woch.* 1944 Aug 25, v. 91 Nos. 33/34 428-9

The author begins by referring to the expansion of the German "Lebensraum" to the East as being responsible for a renewed interest in typhus fever.

The present study deals with 119 convalescent patients aged 19-43 years who were kept under observation till about three months after the onset of the illness. Careful records were kept of the results of simple tests of circulatory efficiency and an analysis is given of the findings before and after exercise tolerance tests carried out at various stages of convalescence. According to the criteria adopted by the author for estimating the significance of these tests it was found that four weeks after the onset of the illness 81.5 per cent. of the patients had a definite degree of circulatory insufficiency 15.1 per cent. had circulatory lability and 3.4 per cent. gave normal responses to the test. Twelve weeks after the onset the corresponding figures were 31.9 per cent. 51.3 per cent. and 16.8 per cent. Abnormal increases, after exercise in the pulse and respiration rates and in the pulse pressure were regarded as reliable indications of circulatory disturbances.

Electrocardiographic examinations were made in 89 cases in 13 of these there was evidence of coronary insufficiency or myocardial damage but at the end of four months only four patients showed any abnormality. Permanent myocardial damage was believed to be of rare occurrence. Among patients observed between the 4th and 12th weeks the lymphocyte count was increased in 68 per cent. and the eosinophile count in 46 per cent.

The blood-sedimentation rate remained high for a long time in most of the cases.

The complications observed among the patients studied were acute glomerulonephritis in one patient this occurred on the 7th day and recovery was complete by the end of seven weeks slight joint rheumatism in two patients urticaria in one and angioneurotic oedema in one These complications had no obvious effect on the circulatory system *John W D Megaw*

NILKA W A Histological Study of the Lungs of Mice Infected with Typhus Rickettsiae. *J Path & Bact* 1945 July v 57 No 3 317-24 12 figs on 4 pls.

The author describes the histology of the lungs of mice inoculated intranasally with murine or epidemic strains of typhus rickettsiae three of the former and seven of the latter strains were used. The methods of preparing the infecting suspensions and of fixing and staining the lungs are described. The following improved method of staining was employed.

Fix lung sections in 10 per cent neutral formol stain in 1 10 000 aqueous methyl violet  $\frac{1}{2}$ -1 hour differentiate in weak acetic acid (2 drops to 100 cc water) until the cytoplasm is unstained counterstain with 1 10 000 aqueous metanil yellow a few seconds acetone xylol mount in Xam (Gurr) or DPX4 mounting medium (Media Mounting Centre)

The paper is illustrated by 12 excellent photomicrographs Large numbers of mice were employed In those allowed to die of the disease there was complete consolidation of the lungs often with a small amount of pleural exudate in the mice that were sacrificed various stages of congestion and consolidation were observed In the congested areas all the blood vessels especially the alveolar capillaries were dilated and the epithelial cells of the alveoli were swollen.

Consolidation was due either to inflammatory oedema or to swelling of the epithelium and packing of the lumen with desquamated alveolar cells and with leucocytes. In many places the vessels and bronchioles were seen to be surrounded by thick cuffs composed chiefly of monocytes.

The usual types of rickettsiae were seen some were extracellular and occurred either in discrete form in clumps in large groups or in masses in the alveoli. Intracellular rickettsiae were most abundant in the alveolar cells whose cytoplasm sometimes was completely packed with cocco-bacilli form or rod shaped organisms in other cells there were masses of granular forms. The endothelial cells of the vessels seldom contained rickettsiae this finding is in sharp contrast with the special invasion of these cells described as occurring in guineapigs inoculated intraperitoneally

Lungs infected by murine rickettsiae were on the average much richer in the organisms than those infected by epidemic strains otherwise the changes caused by the two types of rickettsiae were similar

Secondary infections were surprisingly rare whether or not the mice had been treated by sulphonamides. It is suggested that the rickettsiae inhibit the growth of bacteria *John W D Megaw*

PHILIP C B & KOHLIS G M Studies on Tsutsugamushi Disease (Scrub Typhus, Mite-borne Typhus) in New Guinea and Adjacent Islands. Tsutsugamushi Disease with High Endemicity on a Small South Sea Island. *Amer J Hyg* 1945 Sept v 42 No 2 195-203 4 figs.

This study was carried out under the auspices of the U.S.A Typhus Commission. The authors investigated an outbreak of tsutsugamushi disease which occurred on South Bat Island, situated about 60 miles south of the Admiralty Islands and having its total area of about 46 acres completely

covered by coconut palms under which sparse grass and scattered undergrowth grow. Normally the island is uninhabited except for periodic visits by natives for harvesting the coconuts.

The island swarms with rats—*Rattus concolor browni*—there were 15 pairs of the domestic type which lived in wild conditions. Fruit bats and several species of birds were also found.

The only biting insect that was detected was *Aedes scutellaris*. Large numbers of larval mites were found on the rats—these were *Trombicula deliensis* which H. Womersley has now reported to the authors to be identical with *T. walchi* Womersley and Heatlip 1943. *Schöngastia pusilla* Womersley 1944 was abundant in boot collections but was not found on any of the animals or birds that were examined. It was probably responsible for scrub itch which occurred among the occupying troops. A few specimens of an apparently new species of *Neoschöngastia* were found on a bird, the ground-living rail, *Rallus philippensis*. No other species of mite was found.

Each of five pools of triturated *T. deliensis* from the rats was inoculated intraperitoneally into four white mice and one very large pool of the same larval mites was inoculated into eight mice. Most of the mice died, either within the first two days or later of intercurrent infection so that by the end of 15 days only three mice survived, one from each of three pools. From each surviving mouse a virulent strain of *Rickettsia orientalis* was isolated. One strain which was transmitted through 29 mouse passages killed the animals on the average in 5½ days. It killed nine of ten inoculated guinea-pigs.

Among 41 white periwigs who camped on the island for varying periods between the end of February and the middle of April 1944 and who could be traced afterwards there were 26 definite cases of tsutsugamushi disease. There were two deaths, and most of the patients were seriously ill.

A minority of the campers had slept in hammocks and escaped infection; the majority had slept on cots placed on wooden floors raised from the ground.

The incidence of some of the chief features of the disease is shown in a table. Among the 24 for whom reasonably complete information was available the duration of the fever ranged from 12 to 23 days except for one patient in whose case it lasted 8 days. An eschar was seen in 14 cases; in 8 it was not detected and for the remaining two the information was doubtful. A rash was seen in 11 cases. The results of the Weil-Felix test (*Proteus* OXK) are given for 19 patients; in 8 it was negative but the test was not made till the 35th to the 47th day. In the others the titre ranged from 1-80 to 1-160 or over; most of the tests were made after the 20th day.

This is the first time that *T. deliensis* has been found infected in natural conditions; the only other species hitherto found naturally infected are *T. amushi* in Japan, and *T. fleischeri* in New Guinea.

The high degree of prevalence and virulence of the infection among mites in the island is regarded as being due to the great density of the rat population and the consequent opportunities that exist for rapidly recurring transmissions from rat to mite and from mite to rat.

John H. D. Megaw

KLEIN H. S. An Epidemic of Scrub Typhus. *J. Roy Army Med Corps* 1945 Oct., v. 85 No. 4 187-90.

The author describes the clinical features of an outbreak of scrub typhus which occurred in the months of October November and December 1944 in the Chin Hills of North Burma. Although 225 patients were admitted to hospital during the period the present description deals only with 41 cases among British soldiers; the other cases among Indian troops, are said to have been essentially similar in type.

The incubation period ranged from 4 to 14 days the onset was sudden in about two-thirds of the cases. In the others there were feverish headache and malaise for two or three days before the onset. In the early stages of the illness the disease closely resembled louse-borne typhus. By the third day the patients were seriously ill. Extreme apprehension was a conspicuous feature and it is stated that dread of the disease was universal among the British troops most of whom preferred the Japs. This psychological factor (which has been emphasized by several observers in the Pacific area) was suspected of contributing to the high fatality rate among the British patients of whom five (about 12 per cent.) died whereas only seven deaths (3.8 per cent.) occurred among the 184 Indian patients.

An eschar was seen in 34 per cent of the patients. Generalized lymphadenitis occurred in all the cases but lymphangitis was never seen. All but one of the patients had a rash of a dull red colour. It was macular in 30 cases, maculo-papular in seven, papular in two and morbilliform in one. The rash appeared first on the trunk and soon extended to the arms, legs and face. The palms and soles were never affected.

In all but two of the patients who recovered the termination was by lysis. In four of the fatal cases there was a sudden drop in the temperature with collapse followed by a terminal rise just before death which occurred on the 13th, 14th, 15th and 21st days.

In four cases malaria parasites were found. These were benign tertian in three and malignant tertian in one.

The chief complications were as follows.—Bronchitis occurred in 32 cases and pulmonary infarction in seven. The indications of infarction in four of these were sudden pain in the chest, cough and haemoptysis. In three there were pain and cough without haemoptysis and in one case which was diagnosed after death the only symptom was epigastric pain. Lobar pneumonia occurred in one case in which it was the chief cause of death. Pharyngitis with laryngitis and tonsillitis was present in four cases. Half of the patients had temporary deafness, five had retention of urine and five had severe mental symptoms—delusions, hallucinations or delirium—but all made good recoveries. There was one case of femoral thrombosis also with recovery.

The changes that were found after death in all the fatal cases were oedema and congestion of the brain, small, pale and toxic-looking heart, slight hypostatic congestion of the lungs and enlargement of the intrathoracic lymph glands. There was mononuclear infiltration between the muscle fibres of the heart and slight decrease in the adrenal cortex.

No benefit was observed from the use of penicillin. Sulphonamides were administered to all patients who had chest complications, given also after catheterization. They were believed to have prevented secondary urinary infection.

A fluid intake of 8 to 10 pints was aimed at in spite of the cool situation of the hospital at a height of 5 000 feet. Twenty grains of sodium chloride were added to each pint of liquid. The diet included such articles as bread, biscuits and tinned fruits. 2 400 calories were given daily. Lumbar puncture caused dramatic improvement in four semi-comatose patients whose cerebrospinal fluid pressure was high but it failed in one case in which the pressure was low.

John W. D. Megaw

ANDREW R. A Note on the Incubation Period of Scrub Typhus and its Correlation with Clinical Severity. *Med. J. Australia* 1945 Sept 15, 2, No. 11, 335-6.

In a group of cases of scrub typhus in North Queensland it was possible to fix the incubation period with a considerable degree of reliability. Among 21

cases 10 were classed as being severe (7) very severe (2) or fatal (1) and the incubation period was 12 days in all of them. Among 10 cases classed as moderate (5) mild (4) or very mild (3) there were five in which the period was 15-17 days, in three it was 13 days and in two it was 12 days. In one sub-clinical case it was 18 days.

Weil-Felix tests, carried out retrospectively on 25 other soldiers who had been exposed to similar risk, revealed that two of them had high titre reactions with *Proctos OVK* on the 28th or 29th day after exposure to risk—one of these soldiers gave a history of chilly feeling, headache and myalgia, lasting 12 days and starting 13 days after exposure—his titre was 1-8 000—the other soldier had only headache and coryza, which lasted three days after a presumed incubation period of 18 days—his titre was 1-1 600.

It is stated that 55 cases of scrub typhus, contracted at the same time were treated elsewhere and that only one death occurred in the whole outbreak, in which at least 78 persons were attacked. *John W D Meyer*

DAME L. R. Eye and Ear Sequelas of Scrub Typhus Fever *Bull U.S. Army Med. Dept.* 1945 Nov v 4 No 5 554-7

Among 50 patients seen at a general hospital convalescent (four to six teen weeks average six weeks) from scrub typhus fever 50 per cent. of them had noticeable eye symptoms during the various stages of the disease which proved to be transient and of minor importance. No permanent loss of visual acuity was found to be associated with this disease. In 98 per cent. of these eyes there were some abnormal subjective retinal findings, consisting of enlargement of the blind spots, contraction of the visual fields, and scotomata. The average size of all of the blind spots was 30 by 40 cm., and the largest 33 by 60 cm. There were 7 per cent. of field contractions, and 10 per cent. had scotomata, the largest being one-eighth of the visual field.

"Minor non-specific involvement of the cochlear system was found in only 11 per cent. of the ears at this stage of convalescence although by history 78 per cent. of the ears had had hearing loss or tinnitus. All 50 patients had normal hearing with conversational tones. Involvement of the vestibular system was indicated in 59 per cent. of the ears with caloric stimulation. The of production and chronicity are not definitely known.

"TEXAS" J. M. Field Investigations Pertinent to Bullis Fever The Lone Star Tick, *Amblyomma americanum* (Linnaeus, 1758). Notes and Observations from Camp Bullis, Texas. *Texas Reports on Biol & Med.* 1945 v 3 No. 2, 204-28 3 figs. [17 refs.]

This abstract is supplementary to the one dealing with the author's preliminary note on the present investigations [see this *Bulletin* 1945 v 42, 789]. Full details are given of an exhaustive survey of *Amblyomma americanum* in the Camp Bullis area from June 8 to October 1 1944. This tick has already been found infected with Rocky Mountain spotted fever American Q fever and tularemia in Texas. The chief object of the survey was to obtain large numbers of the tick for the further investigation of Bullis fever with regard to which the author states that "it is quite likely that this disease is rickettsial" and that it is "a new rickettsial disease entity" [The latter statement will be considered by some workers as too dogmatic.]

More than 50 000 specimens of various stages of the tick were collected in the area where it forms more than 85 per cent. of the total tick population, and where it is exceedingly abundant owing to the very large numbers of animals and birds which live in closely preserved conditions. In one case 294 of the

ticks mostly adults were found on a soldier on the head of one deer 910 adults were found and on the head of another there were 1 160 nymphs larval forms were often too numerous to be counted. On occasions as many as one to three thousand larvae but very few adults were found on a fox a jack rabbit and a quail Under a single small juniper tree four collectors picked up 4 086 adults from the thick litter of needle leaves on the ground in the course of a single day

The collection of unfed ticks by dragging the ground with a sheet of whiteannel was found unsatisfactory the plan adopted was to search for spots where the ticks were plentiful a collector seated on the ground would often attract as many ticks as could be dealt with Instead of using a cork for the collecting tube it was found better to tie a sheet of thin rubber obtained from a discarded surgical glove over the mouth of the tube and to cut a small slit in the rubber through which the ticks could be inserted by forceps. On completing the collection the rubber sheet was replaced by a plug of cotton wool.

The methods of collecting fed ticks from animals are described. Tables in the paper give full details of the infestation rates of the various hosts at different seasons Every one of the 15 species of mammals examined was infested by ticks the numbers on small rodents and on the armadillo were negligible. The dominant host of adult ticks was the deer which also harboured large numbers of nymphs and larvae The rabbit fox raccoon, skunk and birds living on the ground or in thickets were heavily infested by nymphs and larvae. Among the birds examined, 32 species were infested and 14 were non infested.

The period of human infestation began in late February the rate increased steadily till the end of May declined slowly till the end of July and then fell rapidly till the middle of August From October to January tick activity was negligible.

[Entomologists who have occasion to carry out tick surveys will find a great deal of useful information in the paper]

John W D Megaw

DOERR W Morphologische Veränderungen bei Wolhynischem Fieber [The Morbid Anatomy of Trench Fever] *Munch med Woch* 1944 Sept 22 v 91 Nos. 35/38 456-8 [10 refs.]

The changes described were found at the autopsy of a German soldier who killed himself by shooting on being discharged to duty from a hospital where he had been under treatment for two months for an illness diagnosed by competent physicians as trench fever About seven months before this illness he had suffered from a moderately severe attack of typhus fever and the changes observed after death could not be distinguished from those commonly resulting from typhus fever The author himself admits that there is some doubt whether the lesions were due to typhus fever or trench fever but he argues at some length in support of the view that trench fever was the cause

John W D Megaw

STÜHMER A Das wolhynische Periodische Fieber [Wolhynian "Periodic Fever (Trench Fever)] *Munch med Woch* 1944 Aug 11 v 91 Nos. 31/32 401-3 1 chart. [11 refs.]

In 1916 the author published an article on A New War Disease Resembling Relapsing Fever In the present paper he describes an attack from which he suffered in 1916 The incubation period could be definitely fixed at 24-25 days. After three short spells of fever with a periodicity of about 7 days there was a long period in which only an occasional slight rise of temperature occurred. From the 12th to the 18th week fever of the undulant type occurred

with a periodicity of about 7 days. The illness lasted for three more weeks, during which there was hardly any fever but there were three spells of pronounced tachycardia.

Recurring bouts of diarrhoea, great weakness and severe shin-bone pains were the other chief features.

*John W D Megaw*

DAVIDS B Jr Beobachtung einer Netzhautblutung bei Wolhynischem Fieber [Retinal Haemorrhage in Trench Fever] *Deut med Woch* 1944 Aug 4 v 70 No. 31/32, 450-51 2 charts.

A German soldier was admitted to hospital after having been in several other hospitals during the preceding month suffering from pain in the head, legs and especially the shins—a provisional diagnosis of Wolhynian fever [trench fever] had been made.

On admission he complained of poor vision, which he had first noticed while writing a letter about three weeks before. About a week before admission the sight of his left eye had become very bad.

On examination a large preretinal haemorrhage was seen the rest of the retina and the bloodvessels being apparently normal. It gradually decreased in size during the following week and he was then transferred from the hospital.

He had no fever on admission nor afterwards, but during the previous month the temperature chart showed a curve resembling that of five-day fever [trench fever]. The differential diagnosis from typhus is discussed—the agglutination test with *Proteus OX19* was negative and there was no rash, while the appearance of the retina did not resemble the condition seen in typhus. As both his parents had died of apoplexy at about 70 years of age the author thinks that there may have been a constitutional tendency to vascular disease.

*J F Corson*

RAETTING H. Die Pyritzerbehandlung des Fünftagefiebers. [The Treatment of Trench Fever by Pyritzer, *Verh Ztschr* 1944 Dec. v 1 No. 3 101-2, 5 charts. [45 refs.]

The author states that his experience in the treatment of 50 patients with pyritzer "a proprietary colon bacillus vaccine for producing artificial pyrexia] confirms the favourable opinions expressed by RHEIMDORF and other observers. He found that definite benefit resulted from a single injection in one-third of the cases, provided that the drug was administered during a febrile paroxysm. Repeated doses at intervals of two days gave no better results than a single injection.

The rationale of the treatment is believed by Rheimdorf to be "an almost specific activation of the processes" [presumably of the immunizing mechanism].

No mention is made of the use of controls [see also this *Bulletin* 1945 v 42, 31].

*John W D Megaw*

## YELLOW FEVER.

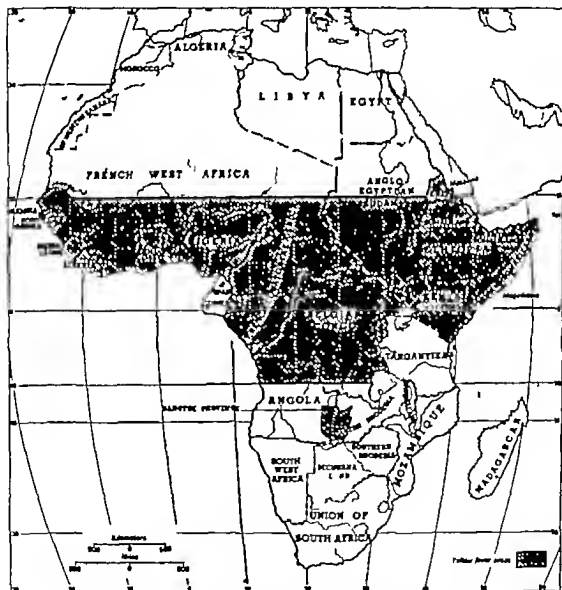
EPIDEMIOLOGICAL INFORMATION BULL. (UNRRA Health Division.) Washington, D.C. 1945 Sept. 30 v 1 No. 16 687-92, 2 maps. Third Report of the Expert Commission on Quarantine [STOCK, P G Chairman]

The delineation of certain parts of Africa and the Western Hemisphere as endemic areas of yellow fever for quarantine purposes, recommended by the

Expert Commission on Quarantine of UNRRA was adopted by the Standing Technical Committee on Health on 11th December 1944 since then the Commission has advised that certain additional areas should be included in the endemic zones

In Africa the additional area is the Barotse Province of Northern Rhodesia in the Western Hemisphere the occurrence of cases of yellow fever in Venezuela and in the States of Minas Gerais and Goyaz in Brazil has led the Commission to recommend an alteration in the previous definition of the delineated areas

The endemic areas are shown in the accompanying maps in South America the western boundary of the endemic area in Colombia and Peru passes along the eastern slopes of the Central Cordillera and the Andes Mountains at a height of 2,000 metres to the boundaries of Argentina and Bolivia.



African Yellow Fever Area delineated by Expert Commission on Quarantine

[Reproduced from *Epidemiological Information Bulletin*  
(UNRRA Health Division.)]





South American Yellow Fever Area delineated by Expert Commission  
on Quarantine

[Reproduced from *Epidemiological Information Bulletin*  
(UNRRA Health Division)]

J. F. CORSON

DE PAULA SOUZA G. H. Yellow Fever Areas. *Epidemiological Information Bull.* (UNRRA Health Division) Washington, D.C. 1945 Sept. 30 v 1 No 16 663-701 [10 refs.]

Under the International Sanitary Convention of Aerial Navigation 1944 the nations concerned agreed to determine whether yellow fever existed in their territories and the Expert Commission on Quarantine of UNRRA defined the endemic areas of the disease *i.e.* where yellow fever exists in a

form recognizable clinically, biologically, or pathologically these boundaries were specified for Africa and South America respectively [see above]

The mouse protection test, viscerotomy, and the examination of animal and insect hosts for yellow fever virus were the methods used. The last of these three methods caused the Ilheus and Itabuna districts in Brazil to be included.

The position is subject to revision from time to time and an area may cease to be considered endemic if satisfactory evidence regarding risk of infection and control of *Aedes aegypti* is furnished.

The Pan American Sanitary Bureau suggested to the Expert Commission that three classes of areas should be distinguished:—(1) Endemic areas where cases have occurred and where conditions favour its recurrence; (2) areas where the risk of becoming infected exists; (3) potentially infectible areas where an *Aedes aegypti* index (i.e. the percentage of houses with breeding foci of *Aedes aegypti*) of 0.4 or higher exists.

The National Department of Health of Brazil pointed out that the infected areas in Brazil varied in character and suggested in detail certain modifications and exceptions.

More information about endemic areas is available for South America than for Africa. In Brazil in 1936 there were 1,559 viscerotomy posts and 32,031 liver samples were examined. In South America an *aegypti* index of 0.4 and less is attainable while in Africa a goal of 1 per cent is regarded as a good first step.

In the Western Hemisphere the Central American countries west of the Canal Zone are no longer endemic areas and the same applies to Mexico and the Caribbean islands. In eastern Panama the endemic area approaches to within 50 miles of the Canal Zone.

No urban outbreak transmitted by *A. aegypti* has occurred in America since 1933 though *aegypti* transmitted yellow fever has often followed jungle yellow fever in Brazil, Bolivia and Colombia between 1934 and 1938 and once in 1942 in the Acre territory in Brazil. The risk of new outbreaks of *aegypti* transmitted or urban-rural yellow fever in South America is now much reduced. A campaign against the mosquito is yielding good results. In 1944 effective work was carried out in 44,859 localities with the result that 42,946 were completely freed. *Aedes aegypti* has been eradicated from eight States and all ports in Bolivia, Colombia, Ecuador, Paraguay and Brazil have an *aegypti* index of close to or actually zero.

Yellow fever still continues in endemic form or as wandering epidemics shifting from one area to another in vast jungle areas. No human case has been found around Villavicencio, Colombia, since 1938 and from protection tests on local wild animals it is thought that active virus no longer exists there. Similar shifting of areas occurred in Brazil. In 1945 an outbreak in the States of Goyaz and Minas Gerais after quiescence for three years caused 101 deaths in the first few months. In July 1945 18 deaths occurred in Venezuela and 14 in Colombia while in May 1945 there were six deaths in Peru and two in Bolivia, east of the Andes in both countries.

In Africa knowledge is based chiefly on surveys. In the western area which extends to the eastern border of Nigeria, *Aedes aegypti* was the vector in urban outbreaks. In the eastern area there is a zone of high incidence of human immunity situated between latitudes 3 and 8 N. and extending from the French Cameroons across French Equatorial Africa into the Anglo-Egyptian Sudan as far as Rumbeck. North and south of this zone there is a lower incidence of immunity. The Barotze Province of Northern Rhodesia is an inland endemic area.

For quarantine purposes endemic areas are extended to the Indian Ocean owing to the danger of eastward spread and the risk to India.

Extensive vaccination of persons exposed to jungle yellow fever anti-mosquito measures and prompt information of jungle infection, should make the defence against yellow fever complete.

J F Corson

## DENGUE.

BOEHMARDT H. Ist das Bessarabienfieber eine neue Krankheit? [Is Bessarabia Fever a New Disease?] *Med. Ztschr.* 1945 Jan. v. 1 No. 4 126-8. [15 refs.]

The author had described a short two-phase fever occurring in Bessarabia as a hitherto unknown disease [see this *Bulletin* 1943 v. 40 839]. He now replies at length to the adverse criticism of this view by MARGOWSKY [see this *Bulletin* 1944 v. 41 988]. He makes out a strong case against the suggestion that the disease may have been trench fever or a fever of the typhoid group, but he admits that serious consideration must be given to the possibility of its being an aberrant form of sandfly fever.

[The controversy over this and other new short fevers in South Eastern Europe is reminiscent of the many discussions relating to short fevers in tropical countries about 25 years ago. In both cases the diseases probably belong to the dengue-sandfly fever group.]

John W D Meyer

## PLAGUE.

MACRAT DICK, J. A Brief Report on Twenty-Six Cases of Bubonic Plague with the Results of Treatment. *J. Roy. Army Med. Corps* 1945 Sept., v. 85 No. 3 105-8.

This report adds one more to the publications on the use of sulphonamide drugs in plague. Its purpose is to give the results of the treatment and to emphasize the desirability of early diagnosis and adequate treatment. Under these circumstances it is maintained that the mortality can be expected to be low. The 26 cases in this series are all set out in detailed tabular form, individually with the precise treatment employed. This averaged 30 to 45 gm. of sulphapyridine per case, the sulphapyridine being combined with antiplague serum in 18 of the cases. The author insists that rest in bed should be strictly enforced as in diphtheria, and the need for this appears to be exemplified by the occurrence of two sudden and unexpected deaths in patients who appeared to be out of danger. He is convinced of the value of sulphapyridine in plague given either alone or in combination with antiplague serum. It is interesting to note that gland puncture becomes negative after 24 hours of sulphapyridine therapy even when a positive result has previously been obtained.

W F Harvey

## CHOLERA.

STOWMAN E. International Quarantine Diseases. I. Cholera. *Epidemiological Information Bull.* (UNRRA Health Division.) Washington, D.C. 1945 Aug. 15 v. 1 No. 13, 551-61.

An account of the distribution of cholera during the present century

GRABAR P & GALLUT J Recherches immunochimiques sur le vibron cholérique IV Essais de purification de la substance hypothermisante de la toxine cholérique [Hypothermy producing Constituent of Cholera Toxin Its Purification] *Ann Inst Pasteur* 1945 Sept-Oct v 71 Nos 9-10 321-6

The characters of the two constituents of cholera toxin were defined in a previous communication [this *Bulletin* 1945 v 42 807] Production of hypothermy and small molecular dimensions were the most notable of the properties found for the second constituent purification of which is dealt with in this article under the headings dimension of the molecule antigenic power and chemical fractionation. A new technique is presented for its extraction of which the detail is as follows —Crude toxin of pH about 5.6 is precipitated with 1.5 ammonia which occurs at about pH 8.6 This precipitate is washed several times with N/100 disodium carbonate until the supernatant fluid gives no precipitate with antilipidic serum It is then totally dissolved by N/10 hydrochloric acid at pH 3.5 In these attempts at purification the following characters have been established for the hypothermy fraction of the cholera toxin It can pass cellophane membranes has no antigenic power is not precipitated by trichloroacetic acid nor by sodium tungstate Therefore it is probably not proteid (as the authors previously thought) it is probably a relatively small molecule thermolabile and liable to be carried down in the course of different precipitations.

W F Harvey

YACOB M & CHAUDHRI J R. A Note on the Presence of 'O' Agglutinins in the Blood of Cholera Patients. *Indian Med Gaz* 1945 June v 80 No 6 291-3

Agglutinins may appear in cholera cases by the second day and are well marked by the sixth day Their titre is not very high and the O agglutinins varied in the present series from 1 in 50 to 1 in 150 Little or no work seems to have been done previously on the persistence of these agglutinins and that is the main object of the present enquiry A knowledge of this point would be useful to the epidemiologist in case it were necessary to conduct a late investigation of an outbreak of cholera in any locality Thirty-seven cases were collected with positive results in 13 and with the possibility of duration up to three and a half months possibly more

W F Harvey

INDIAN RESEARCH FUND ASSOCIATION REP SCIENT ADVISORY BOARD FOR YEAR 1ST JAN TO 31ST DEC 1943 1-7 Cholera Treatment Enquiry under the Director, School of Tropical Medicine, Calcutta.

The efficacy of sulphanilylguanidine in treatment and the preparation of pyrogen free saline solution for injection are the two main subjects of enquiry Every care seems to have been taken in appraising the value of the drug by the use of controls although it is not stated definitely that they were strictly alternate During the year sulphanilylguanidine was administered in 174 cases in the following doses 5 gm on admission, and 2.3 gm every 4 hours after to make a total of 20 gm in 24 hours. A control series also of 174 cases is presented and this series by the criterion of proportion of patients with suppression of urine was identical in number and character with the test series Mortality was only 1.72 per cent in the treated cases and 6.32 per cent in the control series a percentage which is markedly in favour of treatment by sulphanilylguanidine (sulphaguanidine)

Avoidance of accidental temperature and other reactions in the intravenous injection of saline solution is very important and a careful series of clinical

trials and animal experiments with detailed record is presented, to furnish a satisfactory conclusion. As it was difficult to obtain freshly distilled water in quantity measures were taken to make tap water pyrogen-free and suitable for injection. The method adopted was to acidulate 2,000 cc. of tap water with 0.4 cc. of 0.4 per cent potassium permanganate and boil for 2 hours. If the permanganate tinge disappeared, more permanganate was added so as to maintain a trace of colour. At this stage the fluid can be stored, for no organism could grow in the acid water and produce pyrogen. At the time of use as saline solution this water was filtered through filter paper and 5-10 drops of hydrogen peroxide were added to it. Slight heating removed excess hydrogen peroxide and, when cool, the pH was adjusted to 7.1 with caustic soda solution. It may be concluded from the detailed experiments that "pyrogen free water can be prepared by treating water with acid potassium permanganate as by the process of distillation. Other experiments were directed to the determination of optimum pH (7.1) and the effect of oxidizable matter on reaction following injection. The following conclusion is reached—"The reactions following intravenous injections of saline solutions are due to pyrogen (a bacterial product) an oxidizable matter and higher or lower hydrogen ion concentration of the solution."

W F Harvey

INDIAN RESEARCH FUND ASSOCIATION. RES. SCIENT. ADVISORY BOARD FOR YEAR 1ST JAN TO 31ST DEC. 1944 1-4. Cholera Treatment Enquiry under the Director School of Tropical Medicine, Calcutta.

Sulphaguanidine has already been tested and proved successful in the treatment of cholera, but as the trials were in patients seriously collapsed, transfusion of saline solution had to be used also and was a statistical complication. An opportunity has arisen in an epidemic of 97 cases to use sulphaguanidine early and to dispense with the saline solution. There were 53 cases thus treated, leaving 44 cases as controls. The results are recorded under the headings, recovered, died, unknown for sulphaguanidine 79.17 and 4 per cent respectively for the control series 25.73 and 0 per cent. Vibriocidal and vibriostatic tests of sulphaguanidine with culture media showed that it had both properties, but that the bacteriocidal effect *in vitro* was poor.

Tests of another sulphonamide drug, sulphasuxidine (succinyl sulphathiazole) on serious cases requiring intravenous saline therapy with alternate case control were entirely disappointing.

W F Harvey

GUPTA, S. K., CHATTERJEE, B. C., PAUL, B. M. & GHOSE, R. N. Sulphanilylguanidine in Cholera. *Indian Med Gaz.* 1945 June v 80 No 6 288-90.

Preliminary trial had shown the harmlessness of sulphanilylguanidine (sulphaguanidine) and it was accordingly decided to try larger doses than previously. A large series of cases (525) of cholera was available and 263 were treated with sulphaguanidine, the rest being alternate case controls. Saline transfusions were given in both groups as required. The dosage in these cases was 5 gm sulphaguanidine on admission and 2.5 gm. every 4 hours to reach a total of 20 gm. in 24 hours. Beneficial effect was quickly seen and, of 86 admitted with suppression of urine 72 passed urine within 24 hours. This result is contrasted with that in the 72 patients of the control group who also had suppression, of whom only 23 passed urine in 24 hours. Deaths among the 263 sulphaguanidine cases were only 3 whereas 13 out of the 262 controls died. A note is made of seven patients in the control group not expected to recover and developing pre-uræmic symptoms, who did recover when given sulphaguanidine as a last resort. No case treated with sulphaguanidine

developed uraemia. Experiments were conducted also to show that sulphaguanidine had some vibriocidal and vibriostatic action *in vitro*

W F Harvey

INDIAN RESEARCH FUND ASSOCIATION. REP SCIENT ADVISORY BOARD FOR YEAR 1ST JAN TO 31ST DEC. 1943 9-21 Enquiry on the Statistical Evaluation of Anti-Cholera Inoculation in the Madras Presidency under the Director, King Institute, Gulindy, Madras, and the Director of Public Health, Madras.

Up to the present day there have been very few sound statistical attempts to evaluate the effect of any prophylactic vaccine nor does the present careful attempt for cholera conform to the requirement of the alternate case or the alternate village. It is however genuinely statistical and not impressionist. A very full account is given of the conditions under which the trial was made. According to RUSSELL [this *Bulletin* 1925 \ 22, 765 1926 \ 23 191 1927 \ 24 47] whose statistical study is one of the best the epidemiology of cholera in Madras Presidency is closely related to monsoons and there is a seven yearly [six yearly ?] periodicity when there is a marked exacerbation in the incidence of the disease. In Madras the last periodic wave with 70 000 deaths was in 1935-36 and it seems that the present wave began in the first quarter of 1942. Specially devised cards were printed for the present investigation which applied to 2,300 villages of South Arcot. A total of 2,670 cards was obtained relating to 1 283 villages in the district. The reality of immunity against cholera was the main fact studied. Certain special definitions are laid down to give precision to the results. The population of the 1,283 villages was 1,334 016 of whom 392,115 were protected by means of a single dose of Inaba-Ogawa vaccine. An incidence rate per mille of 1.5 for the protected and 17.1 for the unprotected was found which for a 4-fold table gives  $\chi^2$  as 5478.7 and P less than 0.0016. The difference in incidence rates as proof of immunity is undoubtedly significant. Another important point which received attention was that of the time required to establish immunity by vaccination. For cholera a period of six days is prescribed in the International Quarantine Regulations. In the present epidemic it was found that on each of the three days following the date of inoculation the rate of incidence of cholera among the inoculated shows little variation. This rate shows a progressive decline from the fourth day onwards and the minimum is reached on the 10th day after inoculation. The conclusion is arrived at that uninoculated persons in a population at risk are susceptible to an extent of over 10 times in getting cholera as compared with the inoculated persons. When investigation is made of the benefit of vaccination to the inoculated person if he does contract cholera it is found to be negligible. This field study is continuing.

W F Harvey

INDIAN RESEARCH FUND ASSOCIATION. REP SCIENT ADVISORY BOARD FOR YEAR 1ST JAN TO 31ST DEC. 1944 4-21 Enquiry on the Statistical Evaluation of Anti-Cholera Inoculation in the Madras Presidency under the Director, King Institute, Gulindy, Madras, and the Director of Public Health, Madras.

This enquiry follows very closely in method and in text that dealt with in the report of the previous year. It has of course larger figures to deal with although the main findings are much the same. The protected persons are now 709,977 and the unprotected 2,119,568 with an incidence of cholera of 1.57 and 16.20 per 1 000 respectively. In this case the  $\chi^2$  value is 9135.09.

and P is less than 0.0016. In all, 2,350 villages were infected and 627 of these experienced more than one outbreak. The data obtained in the case of villages attacked more than once are used, for analysis of the effects of what are called anticipatory inoculations because the inoculation given in the first outbreak is considered, reasonably capable of furnishing an answer to the question how far previous inoculation confers immunity. Again a significant difference is observed. The incidence rate in the uninoculated persons was 14.2 times the rate in the anticipatory inoculations. A consideration of anticipatory inoculation leads on naturally to that of the duration of immunity conferred by anti-cholera inoculation. One method of arriving at a conclusion was to observe the relative incidence of cholera in the uninoculated and the inoculated groups in a community in the course of an epidemic lasting for a sufficiently long time and noting the interval between the occurrence of cholera in the inoculated and the dates of inoculation. As it is difficult to find an epidemic lasting long enough to allow of this analysis a better method is to study communities of inoculated and uninoculated persons where more than one outbreak has occurred in the community. A table gives the figures which, though small for statistical purposes "point to the presence of immunity in the inoculated population definitely up to ten months and probably also up to twelve months after inoculation."

W. F. Harvey

### BACILLARY DYSENTERY

SCADDING J. G. Sulphonamides in Bacillary Dysentery. Further Observations on their Effects. *Lancet*. 1945 Nov 3 549-53 (29 refs.)

Previously published observations [this *Bulletin* 1944 v. 41 755] suggested that patients suffering from bacillary dysentery showed no significant differences in the duration of their diarrhoea or their length of stay in hospital whether treated with sulphadiazine, sulphapyridine or sulphaguanidine. The present paper records further observations on the sulphonamide treatment of bacillary dysentery. Because sulphaguanidine is the standard drug for the treatment of this disease in the Middle East first succinylsulphathiazole and then sulphadiazine were tested against sulphaguanidine. Secondly observations without controls were made on the effect of smaller doses of sulphadiazine and finally a comparison was made of sulphaguanidine-treated and untreated control cases.

The disease was mild, and in cases where organisms were isolated, 75 per cent. were Flexner infections. The criteria of severity were the duration of diarrhoea before admission to hospital, the number of stools in the 24 hours before admission, and the incidence of fever. The results of treatment were judged by the duration of fever after admission, the duration of diarrhoea, and the total number of days spent in hospital. Treatment, besides sulphonamides, consisted of rest in bed, ample liquid intake, and a bland diet. No toxic complications of sulphonamide treatment developed throughout the investigation. Sulphaguanidine was given in a dosage of 7.0 gm. followed by 3.5 gm. four-hourly reduced after 48 hours if the patient's condition had improved, the average total amount given being about 70 to 80 gm.

Succinyl-sulphathiazole less well absorbed than sulphaguanidine was given in a dosage of 2 gm. five times daily for 3 days then four times daily for 4 days, the course being cut short if there was early improvement. With this course the durations of fever and diarrhoea were very similar to those of the patients treated with sulphaguanidine. The only differences were that the

sulphaguanidine-treated patients were in hospital on the average, 13 days longer than those treated with succinyl-sulphathiazole and showed a greater tendency to recurrence of diarrhoea during convalescence.

In the comparison of sulphadiazine with sulphaguanidine the former drug being readily absorbed was used in dosage of 1.0 gm five times daily reduced after 48 hours if there was improvement to thrice daily. The cases in the two groups were comparable in severity. Those treated with sulphadiazine had on the average slightly shorter fever and very slightly shorter duration of diarrhoea and of stay in hospital than those treated with sulphaguanidine. With reduced doses of sulphadiazine down to 3 gm daily the results were little different the duration of fever and of diarrhoea was very slightly longer but the stay in hospital was rather shorter than in the series treated with larger doses.

In the series of control cases treated by rest and diet only the mean duration of diarrhoea was 5.0 days and of stay in hospital 12.3 days. The corresponding figures for alternate cases treated with sulphaguanidine were 4.4 and 10.8 days. The differences between treated and untreated groups were not statistically significant but it is possible that in the figures for all cases a beneficial effect on a few severe infections was being masked by dilution with a large number of mild self terminating ones and in six Shiga cases there was suggestive evidence that sulphonamide treatment had proved beneficial.

The author gained the impression that sulphadiazine cut short long-continued bacillary-type dysentery on which the poorly absorbed sulphonamides had had no effect. He suggests that in these chronic cases the action of sulphonamides is to combat invasion of the bowel wall by secondary invaders by virtue of their concentration in the blood rather than on the dysentery bacilli by their concentration in the lumen of the bowel where there are likely to be inhibitory substances. On this hypothesis action in acute cases is simply prophylactic against ulceration, either by the dysentery organisms or by the secondary invaders. This would explain the difficulty of detecting any differential effects in mild cases the irregular response in severe cases since the response will depend on what secondary invaders are prominent and finally the fact that small doses of readily absorbable sulphonamides which for other infections would be regarded as prophylactic rather than therapeutic gave as good results in acute bacillary dysentery as larger doses of the poorly absorbable compounds.

*F Murgatroyd*

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## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

DRUCKMANN A & SCHORR S The Roentgenological Manifestations of Amebiasis of the Large Intestine *Amer J Roentgenol & Radium Therapy* 1945 Aug v 54 No 2 145-8 7 figs

Where there is stenosis of the large bowel the radiologist should consider the differentiation of cancer and amoebiasis. Amoebiasis of the colon is either (1) diffuse or (2) localized. In the diffuse type the lesions scattered throughout the colon radiographically resemble those seen in idiopathic ulcerative colitis. In the localized type a more characteristic X ray appearance is seen in order of frequency in the caecum ascending colon sigmoid and rectum. An opaque enema gives a more reliable picture than a barium meal.

The differentiation of a localized amoebic lesion of the large bowel from a cancer can be made on a number of grounds.—The amoebic lesion occupies an extensive segment of the gut the lesions in amoebiasis are frequently multiple while the constriction of the bowel is relatively incomplete and is



intra-abdominal pressure as well as from infectious hepatitis and other forms of hepatomegaly. Some types of pulmonary disease bronchostenosis for example, may give rise to paradoxical movement of the diaphragm. Also in amoebic hepatitis the diaphragm may show no change if the upper portion of the liver is not remarkably involved. In the present group abnormal radiological signs were present in only 15 (45.4 per cent.)

In only two was the complement fixation test of Craig carried out—one was positive the other anticomplementary. There were difficulties in the way of carrying this test out as the material had to be sent away and a long time elapsed before results became available.

P. Manson-Bahr

ALICHA J M, CARPANELLI J B & FERREIRA J A. Abscesso amebiano hepatico absorto en cavidad peritoneal [Amoebic Hepatic Abscess Rupture into the Peritoneal Cavity] *Rev Assoc Med Argentina* 1943 Sept. 18 v 59 No. 563 1043-7 1 fig [44 refs]

MURRAY A M & PHILLIPS G C L. Report of a Case of Amoebic Abscess of Liver Lung, and Brain. *Glasgow Med J* 1945 Oct v 20, No 4 118-18

COUTTS, W E. Urethritis por enteroparasitos. (*Entamoeba histolytica* y *Lamblia intestinalis*) [*Entamoeba histolytica* and *Giardia intestinalis* in Urethritis.] *Rev Chilena de Hig y Med. Preventiva*. 1945 Mar v 7 No. 1 3-5 English summary (8 lines)

The author relates that in an earlier publication he has called attention to the frequency with which trichomonas and spirochaetes can be detected in urethral discharges. In the present paper he describes two cases of urethritis in the discharge of one of which *Giardia intestinalis* was discovered and in that of the other *Entamoeba histolytica*. In both cases a cure was obtained by injections of pergonon

C M Wrayon

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

DEWAR, H A & WALMSLEY R. Relapsing Fever with Nephritis and Sub-  
arachnoid Haemorrhage. *Lancet* 1945 Nov 17 630-31

The description of a fatal case of (presumably) tick-borne relapsing fever in a soldier convalescent from amoebic dysentery. The patient had spent most of the previous four months in the western desert of Egypt.

The attack developed whilst he was still in hospital after his stools had become negative for *Entamoeba histolytica* and treatment with carbarsone tablets (0.25 gm. twice daily by mouth) had begun. On the 5th day *Spirochaeta recurrentis* was found in large numbers in a blood film. On the 7th and 8th days the blood was negative, but the patient was severely ill and his blood urea rose to 360 mgm. per 100 cc on the 10th day.

After only one bout of fever nephritis and severe epistaxis supervened and the patient died on the 12th day as the result of a subarachnoid haemorrhage.

Autopsy was performed 2½ hours after death and attempts were made without success, to detect the presence of spirochaetes in the bone-marrow, brain and spleen both by examining smears and inoculation into mice. Microscopically as well as *in vivo* the most striking feature of the nephritis

was its intensely haemorrhagic character which together with the epistaxis and the perirenal and subarachnoidal haemorrhages suggests a general haemorrhagic tendency in this case.  
E Hindle

[No information as to the species of tick responsible for transmission is given and the evidence is presumptive only similarly it is assumed that the organism was *S. recurrentis* but no detailed investigation was possible.—Ed.]

LAHIRI M N Leptospirosis without Jaundice. *Indian Med Ga* 1945 July \ 80 No 7 338-7

The author describes the clinical symptoms of a patient admitted to hospital for fever headache and agonizing pains all over the body. He was seen on the eighth day of illness. The urine showed total absence of bile salts and pigments but a trace of albumin was present. Cultures and animal inoculation of the patient's blood were negative but the serum reacted to a titre of 1:1,280 with a local strain of leptospira.

A total of 225 samples of sera sent in to the Haffkine Institute Bombay for Widal tests were examined for leptospira by serological tests against three strains. One serum showed a titre of 1:640 and as it had been sent for Widal test jaundice was presumed to have been absent.  
E Hindle

MOHANTY J K The Occurrence of Leptospirosis in Orissa. *Indian Med Ga.* 1945 July \ 80 No 7 337-8 [11 refs.]

The record of a patient admitted to hospital for the treatment of haematemesis melaena and jaundice. The agglutination reaction against a classical strain of *Leptospira icterohaemorrhagiae* was negative. Nevertheless the urine when centrifuged showed the presence of spirochaetes closely resembling leptospirae. Animal inoculations were not possible.  
E Hindle

LAHIRI M N The Unsuitability of White Mice for Studies of Leptospirosis. *Indian Med Gaz* 1945 July \ 80 No 7 338-9

Three-weeks-old Haffkine Institute inbred mice and also Javanese mice were inoculated with varying doses of two virulent cultures of *Leptospira icterohaemorrhagiae* in batches of three.

In the first series out of 36 mice all survived except one and in the second series of 30 Javanese mice there were only two deaths from the infection. In addition six Swiss mice were tested and all survived. The control guinea pigs all succumbed between the fifth and seventh day after inoculation.

These experiments therefore do not support LARSON'S results (see *Bulletin of Hygiene* 1942 v 17 144) at least so far as laboratory studies of leptospirosis in India are concerned.  
E Hindle

## HELMINTHIASIS

MAZZOTTI L. Presencia de huevecillos de varios helmintos diferentes del *E. vermicularis* en la region perianal de individuos examinados en Mexico para investigar oxiuriasis. [The Presence of Ova of other Helminths in the Perianal Region of People in Mexico examined for Oxyuriasis.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 June \ 6 No 2 131-5 English summary (4 lines)

The examinations were made in four seaside localities with a tropical climate and in Mexico City which has a temperate climate. 1,260 schoolchildren were

examined in the former places and 1,229 children and 500 adults in Mexico City. GRAHAM's method with Scotch cellulose tape [this *Bulletin* 1942 v 39 780 1943 v 40 617] was used.

The results are given in detail in a table. Among the 2,889 persons examined helminth ova other than those of *Enterobius vermicularis* were found in 188 (6.6 per cent.) they included ova of *Ascaris lumbricoides* (96) *Trichuris trichiura* (100) hookworm (6) *Taenia* (26) and *Hymenolepis nana* (3).

The children in the tropical localities had a greater incidence (up to 20 per cent.) than the persons in Mexico City (2.6 per cent.). The author discusses the point whether the proglottides of *Taenia solium* migrate through the anus.

J. F. CORSON.

McMULLEN, D. B. & BEAVER, P. C. Studies on Schistosome Dermatitis. IX. The Life Cycles of Three Dermatitis-producing Schistosomes from Birds and a Discussion of the Subfamily Bilharziellinae (Trematoda: Schistosomatidae). *Amer. J. Hyg.* 1945 Sept., v 42, No 2, 128-54 1 fig & 3 pls. [35 refs.]

"1 Techniques used in detecting schistosome infections in birds are described.

"2 In experiments with three dermatitis-producing schistosome cercariae *C. phryellae* Talbot, *C. elae* Miller and *C. stagnicolae* Talbot adult schistosomes have been recovered from birds. After examining these trematodes and the literature on members of the subfamily Bilharziellinae Price 1929 the adults of *C. phryellae* Talbot were determined as *Trichobilharzia phryellae* (Talbot) (syn. *Pseudobilharzia quercusculae* McLeod) n. comb. the adults of *C. elae* Miller as *Trichobilharzia ocellata* (La Valette) (syn. *T. konarskyi* Skrjabin and Zakharov) and the adults of *C. stagnicolae* Talbot as *T. stagnicolae* (Talbot) n. comb.

"3 A revision of the generic diagnosis of *Trichobilharzia* is proposed. This reduces the genus *Pseudobilharzia* Elmont to synonymy with *Trichobilharzia*. Since it is difficult to differentiate species in this genus on the basis of adult morphology it is concluded that the eggs may be one of the most reliable characters for this purpose.

"4 While no attempt has yet been made to find these three common species in resident or migratory birds in the vicinity of infested beaches it is evident from earlier studies that the most common natural hosts are migratory birds, and the present study has shown that *Trichobilharzia ocellata* and *T. phryellae* develop in ducks and other birds while *T. stagnicolae* was found to reach maturity in canaries only.

5. In all three species eggs are produced in about 2 weeks after infection and there is some evidence that the infection does not last longer than 1 or 2 months.

6. Protecting beaches from flocks of migrating birds especially in the fall may be of value in preventing schistosome dermatitis on bathing beaches.

HARRIS, J. R. & HICKEY, M. D. Occurrence of the Diphylobothriidae in Ireland. [Correspondence.] *Nature* 1945 Oct. 13 447-8.

This paper further discusses the occurrence of plerocercoids of Diphylobothriidae found by the authors [this *Bulletin* 1944 v 41 858] in trout in Poulaphuca reservoir near Dublin by DUGUID and SHEPARD [*ibid* p. 857] in trout in a South Wales reservoir and by GIBSON [*ibid* 1945 v 42, 396 see also LYNWORTH, *ibid* p. 397]. BAYLIS [*ibid* p. 806] has examined adult Diphylobothriids reared experimentally in dogs from the Dublin and South Wales

plerocercoids and considers that all these plerocercoids and also the adults obtained from gulls and cormorants by the authors mentioned above probably belong to the Diphyllobothrid species *D dendriticum* (Nitzsch) which is normally parasitic in gulls although those found in the cormorants may be *D ditremum*. The possible confusion of the plerocercoids of these bird species with those of *D latum* of man required further investigation because it is very difficult to distinguish from one another the plerocercoids of different species of Diphyllobothridae. The difficulty is increased in Eire because *D latum* does occur there. Harris and Hickey here record references to its occurrence the first record being that of BELLINGHAM—and O BRYAN—(*Ann Mag Nat Hist* 1844 v 14 251). To these records Harris and Hickey add another recent one. They received from Dr T V McLoughlin a specimen of *D latum* recovered from a boy aged 14 who had eaten perch from Gardice Lake Co Leitrim. Harris and Hickey searched 79 perch from this lake for plerocercoids and found from 1 to 8 plerocercoids per fish in 35 of the 79 perch examined. Similar plerocercoids were found in two perch from Lough Allen Co Leitrim. Plerocercoids from the Gardice Lake perch were given by mouth to two adult dogs and from both of these dogs which were given 2 and 8 plerocercoids respectively adult Diphyllobothrids were recovered. The two adults obtained from the dog given 2 plerocercoids were specimens of *D latum*.

Harris and Hickey compare the plerocercoids obtained from trout of Poulaphuca reservoir Dublin (namely those of *D dendriticum* of gulls or *D ditremum* of cormorants) with those from the perch from Gardice Lake from which they experimentally reared *D latum*. They note the following differences—

The plerocercoids of *D latum* were opaque and dull white and were only sluggishly motile. They seldom relaxed sufficiently to lose their typical irregular deeply wrinkled appearance. When they were killed in tap water the scolices usually remained invaginated and showed deep wrinkles. Of the 81 plerocercoids found in the perch of Gardice Lake 71 were found in the skeletal muscles and only 10 in the peritoneal cavity or abdominal viscera. There was no inflammatory reaction around them.

The plerocercoids of the trout from Poulaphuca reservoir (of the bird species) were translucent glistening white and actively motile. They showed no wrinkling except when they were strongly contracted. When they were killed in tap water they invariably relaxed and evaginated and wrinkles were never present although some showed segmentation. Out of the 198 infested trout examined only one had plerocercoids in the skeletal muscles (two were found in it) in all the others the plerocercoids were in the viscera or subserous tissues of the abdominal cavity. Around them there was often an inflammatory mass of blood stained granulation tissue.

The authors examined fish from other Irish waters namely reservoirs in Wicklow and Dublin Counties Lough Mask Co Mayo four Lakes in Connemara, Co Galway and Lough Eske Co Donegal. Plerocercoids superficially resembling those found in trout from Poulaphuca reservoir (i.e. presumably plerocercoids of Diphyllobothridae parasitic in birds and not in man) were found in trout (*Salmo trutta*) salmon (*S salar*) and char (*Salvelinus colii*) G. Lapage

GRASA A. Alergia y diagnóstico biológico de la hidatidosis. [Allergy and the Biological Diagnosis of Hydatid Disease.] *Arch Uruguayos de Med Cirug y Especialidades* 1945 June v 26 No 6 538-59 [75 refs.] English summary

It is not possible to abstract in detail this review of an extensive bibliography of this subject. The author considers much South American work which is not readily accessible and also incorporates his own experience. Many

of the papers considered are also reviewed by TALIAFERRO (*The Immunology of Parasitic Infections* 1929 Century Co. London and New York)

In the course of his discussion of the technique and significance of the immediate and delayed (Casani) intradermal reaction, GRAZIA reminds us that tuberculosis is among the conditions other than hydatid disease which may give rise to falsely positive intradermal reactions to the injection of hydatid fluid. He quotes the work of DABOWSKY (cited by MOLLOW see this *Bulletin* 1931 v 28 205) who obtained a high percentage of positive intradermal reactions with hydatid fluid in tuberculous children [cf DAVIS HARRELL and KING *Bulletin of Hygiene* 1946 v 20 673]. GRAZIA states that statistics show that positive Casani reactions are most numerous in subjects with hydatid cysts of the liver and next most numerous in those with cysts of the lung. In his experience strongly positive Casani reactions may occur even when hydatids of the liver and lung are suppurating or are calcified but they are often negative in subjects with cysts in the bones or brain.

The technique and significance of the Prausnitz Kustner test applied to hydatid disease is discussed. GRAZIA obtained a positive Prausnitz Kustner reaction in only one of many subjects who gave a strongly positive Casani intradermal reaction but he considers, nevertheless that the passive transference of hypersensitivity is possible.

Human hydatid fluid has he considers a very low antigenic power. The sterile cysts of the liver and lung of sheep give the best hydatid fluid for use as antigen. FERNANDEZ ITURRAT and CALCAÑO [see this *Bulletin* 1924 v 21 206] obtained, however just as good results with human hydatid fluid as with fluid obtained from oxen and sheep. They maintain that the antigenic power of the fluid should be tested both on healthy subjects and on subjects with hydatid cysts before it is used. Discussing the nature of the substance which provokes the intradermal reaction GRAZIA recommends for use either 0.1 cc. of hydatid fluid previously tested, or the protein fraction obtained by DEXNIS (*J. Parasitology* 1937 v 23 60) who isolated a protein by precipitation with 5 per cent. trichloroacetic acid and obtained with it intensely positive reactions with erythema prolonged for 48 hours and oedema lasting 4 to 5 days. [See also the polysaccharide and protein obtained and tested by PIROSKY *et al* (this *Bulletin* 1943 v 40 474)]

The author next discusses the blood eosinophilia and the local eosinophilia which may both result from the injection of small amounts of hydatid fluid into subjects with hydatid cysts. In hydatid disease the blood eosinophilia is not significant unless it exceeds 5 per cent but values higher than 5 per cent may occur when infestations of the muscles and blood with other parasites are present and also when there are skin affections, allergic conditions etc. [cf DIXON and HARGREAVES (this *Bulletin* 1945 v 42, 907) who discuss the results of their study of 284 cases of cysticercosis due to *Taenia solium* and quote the opinion of GORON (this *Bulletin* 1943 v 40 65) that Continental workers have attached too much importance to blood eosinophilia, which Dixon and Hargreaves found in only 10 per cent of their cases. They agree with MACARTHUR (this *Bulletin* 1934 v 31 384) that such deviations from the normal eosinophilia of the cerebrospinal fluid as may occur have no diagnostic significance and that the cerebrospinal fluid generally remains unaffected even when there is gross cerebral cysticercosis. GRAZIA, on the other hand, refers in the paper here reviewed, to the view of PARVU and LAURKY (*C.R. Soc. Biol.*, 1909 v 66 467) that "the eosinophilia of the cerebrospinal fluid which is so characteristic of cerebral cysticercosis" (see GRAZIA & SCHERONE this *Bulletin* 1942, v 39 705 and SELMAN *ibid* 1945 v 42, 816) is not present in hydatid disease. GRAZIA insists that both the relative and the absolute eosinophilia of the blood must be considered. He found that the subcutaneous or

intradermal injection of even as much as 10 cc. of hydatid fluid did not cause in healthy subjects a significant increase of eosinophils in the blood but in subjects with hydatid disease repeated injections of hydatid fluid caused eosinophilia in proportion to their sensitivity as indicated by the degree of the Casoni reaction. One subject tested by Graña showed a local eosinophilia so intense that the fluid in the local blister contained 29 per cent of eosinophils. Although MOLLOV (*loc cit*) does not attribute diagnostic value to this induced eosinophilia Graña considers that it has real diagnostic value if it is considered in relation to the other blood changes provoked.

The author next reviews some of the literature on the complement fixation (Ghedini Weinberg) reaction. Like the Casoni reaction it may give false positives in subjects suffering from haemangioma or primary cancer of the liver (see MOLLOV *loc cit*). PARVU and LAUBRY (*loc cit*) record that in subjects with cerebral hydatids the complement fixation reaction done with cerebrospinal fluid is positive although it is negative when it is done with blood.

Discussing heterophil antibodies Graña refers to the work of CALCAGNO (*Boletines y Trabajos de la Acad. Argent. de Ciruj.* 1939) who studied the effects of the injection of hydatid fluid into subjects harbouring hydatid cysts and called this procedure the biological therapy of hydatid disease [cf. RIVAS GÓBICH and MANTILLA this *Bulletin* 1945 v 42, 910]. Graña (*Dia Méd.* Buenos Aires, 1943 v 14, 1092) [see also this *Bulletin* 1944 v 41, 764] has observed in the serum of subjects thus treated a notable increase of haemolysins and agglutinins for the erythrocytes of sheep and has obtained agglutination in dilutions of serum as high as 1:2048 and haemolysis in dilutions of 1:4096 using the technique of PAUL and BUNNELL (*Amer. J. Med. Sci.* 1932 v 183, 90) for the diagnosis of infectious mononucleosis. Graña noted great variability in the titres of heterophil antibodies shown by different individuals harbouring hydatid cysts in relation to the same antigen. He has found [this *Bulletin* 1944 v 41, 764] that in rabbits and in subjects without cysts injection of hydatid fluid does not cause an increase of agglutinins and haemolysins to erythrocytes of sheep while in subjects with cysts the rise in these heterophil antibodies is strictly parallel to the degree of hydatid allergy shown by the Casoni intradermal reaction done upon them. Graña (*Arch. de Med. Ciruj. y Especialidades* 1944 v 24, 471 and *Clínica e Inmunología* Edit. Espasa Calpe 1944) found that the formation of these heterophil antibodies is rapid and intense and that this serological reaction has a certain diagnostic value (see also Graña *Medicina* Buenos Aires 1945 *in the press*). Graña has also seen a notable increase of agglutinins and haemolysins to sheep erythrocytes in the sera of sensitive subjects into whom extracts of *Ascaris lumbricoides* of the pig have been injected (*Rev. Brasileira Biol.* 1945 v 5, 81). The author then describes what he calls the triple response to the introduction of antigen. If the eosinophilia exceeds 5 per cent and the intradermal and complement fixation reactions are positive one can be sure that the subject has a hydatid cyst. If all or some of these reactions including titration of the serum against the erythrocytes of sheep are negative and if we wish to increase the efficacy of the reactions the triple response can be tried. Hydatid fluid (2 cc.) is injected intradermally into separate sites in the skin each day for five days if after 96 hours or with more certainty after 48 hours from the beginning of the reaction a negative complement fixation reaction has become positive and the eosinophils have exceeded 5 per cent it is necessary to suspect hydatid disease because subjects without cysts do not react in this way in so short a time (see Graña *Arch. de Med. Ciruj. y Especialidades* 1944 v 24, 471 and *Medicina* Buenos Aires 1944 v 4, 290). Five to ten days after the last injection the late response shown by increase of agglutination

of sheep erythrocytes is studied, and if the titre of this is above 1/32 by the technique of Paul and Bunnell there is further reason for the diagnosis of hydatid disease.

The author next discusses histaminaemia in hydatid allergy. Graña *et al.* (*Medicina*, Buenos Aires, 1943 v 3 98) found that histaminaemia in subjects with hydatid disease is very variable. High values were found in subjects with hepatic hydatid, three of whom had calcified cysts. One subject with a small calcified hydatid had marked digestive troubles and his histaminaemia rose to the titre of 48 gammas per cent. Such high values suggest a relation to the increased number of eosinophils in the blood, for CODE (*J. Physiology* 1937 v 89 257) suggested that the eosinophils carry the histamine. RANDOLPH and RACKEMANN (*J. Allergy* 1941 v 12, 480) could not, however accept this view and Graña and his collaborators found no relation between the absolute or relative number of eosinophils and the degree of histaminaemia, nor did he find histamine in the vesicle produced by injection of hydatid fluid, although in this there were 29 per cent. of eosinophils.

Clinically subjects with hydatid disease can show various signs of classical allergy such as asthma, urticaria, angioneurotic oedema and other symptoms which rapidly yield to desensitization with hydatid fluid. The author refers to instances of asthma which were clearly of hydatid origin and to the provocation of a severe asthmatic state by the injection into a subject with a hydatid cyst of the lung of excessive quantities of hydatid fluid. JAUREGUI and SOTO (*Alergia hidatidea pulmonar* Monografía Imprenta Rosgal, Montevideo 1941) interpret radiological shadows in the lung near a hydatid as of hydatid origin. There are many instances of chronic and stubborn urticaria which have vanished when the hydatid cyst has been removed. In one subject cited by Graña it disappeared after the first desensitizing injection of hydatid fluid. Various other symptoms may also disappear after similar injections. Among the most notable results of this biological therapy (see Calcagno above) is the rapid disappearance of dyspeptic pains and symptoms of a hepatic or biliary type in subjects with calcified liver hydatids and without any lesion of the gall bladder (cf Graña, *Bol. de la Soc. de Ciruj. de Montevideo* 1943 May and *Dis. Med.* Buenos Aires, 1943 v 14 1092, and *Prensa Med. Argentina* 1944 v 31 No 16).

Discussing anaphylactic shock due to the rupture accidental or during surgical operations, of hydatid cysts and the consequent rapid and massive absorption of antigen by subjects previously sensitized, the author quotes the view of CHAFFARD *et al.* (*C.R. Soc. Biol.* 1909 v 67 499) that this sensitization is slow and chronic being produced by the passage of hydatid fluid through the wall of the intact cyst or through small fissures in the cyst. Death may result from this shock. D *v.* (*Rev. de Chir.* 1911 v 1 153) describes post-operative hydatid intoxication which corresponds to anaphylaxis due to reabsorption of hydatid fluid—this kind of phenomenon does not occur during operation, because the general anaesthesia inhibits the signs of shock, which may be benign or severe. Graña suggests that the study of experimental shock shows that hydatid fluid is a primary toxin to cells, and it is possible that what is interpreted, in man, as pure anaphylaxis may be a combined result of anaphylactic phenomena and primary toxicity of hydatid fluid.

The author then discusses experimental hydatid anaphylaxis and reviews literature on this question which shows he thinks that there has been difficulty in producing experimental anaphylaxis. LEVAIRE thinks that this difficulty may be due to the fact that hydatid fluid is poor in proteins. DESAY and MAROTTA (*Rev. de la Soc. Med.* 1912, v 20 p. 373) produced shock in dogs by the intravenous injection of 20 cc. of hydatid fluid, and GUSTI and HCG (*II Congreso de Medicina* Buenos Aires, 1922, v 1 691) confirmed this and also

produced shock by injection of hydatid fluid which had been either boiled or ultrafiltered. They found that the histamine titres were so small that the effect of this substance could be ignored. Graña has confirmed the results of Giusti and Hug. Graña and his colleagues (*Rev de la Soc Argent de Biol* 1943 v 19 444 and *Amer J Physiol* 1945 v 143 306) showed that in some dogs the histamine increased in the blood during the shock while in others the histaminaemia increased so that histamine could not have been the cause of the shock. A substance can however be extracted from hydatid cysts which is responsible for the shock this is not a protein it is resistant to heat and is precipitated by acetone. A dose of 60 mgm. produces in dogs a profound shock which is followed by desensitization. *G Lapage*

DAVIS O T HARRELL G T & KING E S The Effect of Simultaneous Tuberculous Infection on Experimental *Trichostrongylus* Infestations in Guinea Pigs. *Amer J Med Sci* 1945 June v 209 No 6 758-64 3 figs.

This paper is reviewed in *Bulletin of Hygiene* 1945 v 20 673

## DEFICIENCY DISEASES

TROWELL H C & MUWAZI E M K Severe and Prolonged Underfeeding in African Children. (The Kwashiorkor Syndrome of Malignant Malnutrition) *Arch Dis in Childhood* 1945 Sept v 20 No 103 110-16 5 figs [30 refs]

The name kwashiorkor is a tribal word from the region of Accra in the Gold Coast and is not understood outside this area, but the syndrome for which it stands is found in many parts of Africa and possibly elsewhere. This syndrome includes a pale red skin with brownish hair a crazy pavement dermatosis wasting oedema anaemia lowered plasma albumin and raised globulin a gastro-intestinal defect seen radiographically as gross segmentation of the small gut and marked fatty degeneration of the liver. In its advanced stages the syndrome is notably refractory to treatment. The syndrome has frequently been taken to be a manifestation of pellagra but this view is no longer tenable. The anaemia at least in Uganda is macrocytic and hypochromic megaloblasts are seldom if ever seen in films of peripheral blood or bone marrow.

Adding to the previous descriptions of the senior author Trowell and Muwazi during 1945 examined 180 children 126 of them out patients and 54 in patients at Kampala Uganda. After the sixth month about three-quarters of all cases attending the clinic showed signs of the syndrome. Plasma proteins were determined in 20 patients in most cases the plasma albumin was low and the plasma globulin was high so that the albumin/globulin ratio was low in every case this ratio was below the mean albumin/globulin ratio for normal children in many cases it was less than 1.

Malaria parasites were found in 119 of the 180 children. Among these same children were 17 probable cases of congenital syphilis. Of the 54 cases in the wards of the hospital 12 had pneumonia, 4 bacillary dysentery, 1 amoebic dysentery, 14 ankylostomiasis, 4 ascariasis and 6 giardiasis. Thus in the tropics kwashiorkor is seldom seen uncomplicated by infection of which the most important is malaria. The syndrome has however been observed in South Africa almost uncomplicated by tropical disease.

The authors think that the syndrome may be the same as severe marasmus in European children with a few variations due to the peculiarities of the



African diet. They also point out that it is almost impossible to distinguish the syndrome from coeliac disease, although in "kwashiorkor" oedema is far more common and many more cases proceed rapidly to marasmus and death.

A trial of denoated hog's stomach in six cases gave encouraging results; one case is described in some detail. This child, who had severe oedema, showed no improvement during a fortnight on a high-calorie, high-protein diet plus thiamin and nicotinic acid, nor during a further 4 days with daily injections of liver extract. Denoated hog's stomach given by mouth was followed by a remarkable and rapid improvement. [See also GILLMAN *et al* this *Bulletin* 1944 v 41 1057 1945 v 42, 748 1946 v 43, 59]

The authors suggest that the syndrome should be called "malignant malnutrition."  
H E Harding

QUITTER, F. Beiträge zum Pellagraproblem. [Contributions to the Problem of Pellagra.] *Deut. Tropenmed. Ztschr.* 1944 Jan. 1 v 48 Nos. 1/2, 18-25 [11 refs.]

The author is convinced that pellagra in Rumania presents several differences from the disease elsewhere—so much so that he regards the so-called pellagra in some of the Balkan districts as pseudo-pellagra and not true pellagra at all. In Rumania the disease was present where maize was much used, and when other grains took its place pellagra diminished. On the other hand cases are seen in Rumania in which maize plays no part and the disease is seen in the better nourished and well-to-do families. In Rumania the disease is typically seasonal—cases begin to appear at the end of February and the beginning of March, and increase until the summer when they begin to fall in numbers by late autumn and the start of winter then disappear altogether. The symptoms typically are tiredness, apathy and later—often much later—glossitis, burning sensations in the throat, digestive disturbances, erythema of hands, feet, face and neck. There may be no relapse the following year even though the patient remains at home and in no way changes his mode of living. Mental disturbances appear late.

The author does not regard pellagra as purely an avitaminosis, because it is rare to see more than one case in a family (of 79 patients in 1941 only two were members of one family) and cure takes place without increase of vitamin.

There may be a constitutional endocrine factor and some cases wear up quickly when sexual hormones are given. In others there is evidence in favour of some sensitizing factor as photosensitivity: the gastritis may be of a "constitutional" nature, when relapse is likely to occur or it may be accidental and fortuitous and, if so, once cured it is not likely to return. Allergic diseases are commoner in females says the author and 91 per cent of his patients were women, and treatment with specific anti-allergics, as Reticulin or Torantil [both are prepared from animal tissues] yielded good response. The allergy might be endogenous (auto-intoxication) or exogenous, perhaps due to some toxin in spoiled maize.

The author quotes several cases which improved on Reticulin. One a severe case may be cited. A man, aged 20 years, ill each spring for the past two years, worse this year—is apathetic and will not answer questions, has erythema of the face, lips swollen and painful, tongue has many painful fissures, burning sensation in throat and stomach, such that he can take scarcely any food. He was given Reticulin, 2 cc. every other day and improvement started after the fifth injection—the throat and stomach symptoms were eased, the general state was better and three weeks after completion of the course the hands and feet showed only slight pigmentation—he was much more alert and his only complaint was of feeling fatigued sooner than he used to at his work.

The author regards nicotinic acid as having the properties of a vitamin daily administration of 200-300 mgm led to definite improvement in 12-14 days. It is not an anti pellagra vitamin but acts as a constituent of cozymase.

Other patients were treated with Decholu. 10 cc injections of 20 per cent strength on alternate days. Here again an example may be quoted: a man of 53 years with lassitude, erythema, glossitis, gastritis, severe diarrhoea, burning pain in the throat. Six injections were given. At the end of the first week his subjective symptoms were vastly improved and by the end of the course he was in general cured. Some redness of the skin remained but that was all.

Neither those treated with Reticulin nor those with Decholin changed in any way their mode of living so that the results may definitely be ascribed to the treatment adopted.

H. Harold Scott

NICHOLLS, Lucius. *Tropical Nutrition and Dietetics.*

This book is reviewed on p. 165

## HAEMATOLOGY

DENHOFF, E. *Hematologic Values of American Soldiers Stationed in the Tropics*. *J. Lab. & Clin. Med.* 1945 Oct v 30 No 10 874-82.

American medical officers stationed in the South west Pacific had more than once remarked in general terms that each month the red blood cell count seems to be lower and the incidence of eosinophilia increases. The author resolved to put this supposition to the test and examined the blood of 655 American soldiers admitted to hospital and of a small number (33) of healthy soldiers. The former included 142 who had been stationed in the tropics for 6 months, the main causes for admission to hospital being bacillary dysentery and acute infective hepatitis. 211 who had been out for 12 months, the causes of admission being respiratory diseases, bacillary dysentery and malaria, and 302 who had been out for 18 months, filariasis and malaria were the main diseases in these. In these three groups respectively, the average red cell counts and haemoglobin estimations (by the Tallqvist scale) were 4 710 000 per cmm and 88 per cent., 4 560 000 and 88 per cent. and 4 390 000 and 84 per cent. As regards the controls, the average of 14 recent arrivals was 4 970 000 and 95 per cent. haemoglobin and of these together with 19 others after a year's stay 4 770 000 and 91 per cent. at the end of two years the average was 4 400 000 and 84 per cent.

Among those in Group I there was only one (0.7 per cent.) noted as a case of borderline normocytic anaemia. In Group II there were 13 (6.7 per cent.) and in Group III 29 (9.6 per cent.). Eosinophilia of 9 per cent. or over was present in 1, 7 and 26 (or 0.7, 3.3 and 10.1 per cent.) respectively in the three groups, accounted for by helminthic infestations or dermatoses. For 9 others no explanation was found.

Of 100 patients garrisoning filaria free islands, 8 had this degree of eosinophilia, while of 156 on an island where filariasis was endemic 18 (11.5 per cent.) had eosinophilia. Of 140 healthy soldiers on filaria free islands 5 (3.5 per cent.) had eosinophilia compared with 40 (28.1 per cent.) of 142 exposed to filariasis.

It will be seen therefore that the erythrocyte count and the haemoglobin values fell with length of service and it was thought that lack of thiamin, riboflavin and ascorbic acid were contributory factors. Monotony and lack

of palatability of the food were also part causes, the food itself being adequate. The incidence of true anaemia was slight. It is noteworthy that a high incidence of eosinophilia was present in healthy soldiers who had been stationed in a filaria-endemic island, although they presented no clinical evidence of infestation. [See also this *Bulletin* 1945 v 42, 1020] *H Harold Scott*

HOLMES E. G. Observations on Oedema occurring during the Course of Macrocytic Anaemia. *Brit Med J* 1945 Oct. 27 561-4

Oedema and ascites in tropical macrocytic anaemia have usually been attributed to cardiac insufficiency but in the present series of 38 cases of macrocytic anaemia in East African troops in the S.E. Asia Command, oedema and ascites which occurred in 12 did not appear except in one, until as a result of treatment, the blood count had risen considerably and at a time when other signs which could be attributed to cardiac decompensation were entirely absent. As the manufacture of haemoglobin involves the synthesis of protein as well as the production of the iron-containing haem molecule observations were undertaken to ascertain whether any diminution in plasma protein occurred which might explain the oedema and ascites in such cases. Oedema is said to occur if the total protein falls below 5.5 per cent. or the albumin below 2.5 per cent. The osmotic pressure of the serum depends upon the sum of the osmotic pressures of its albumin and globulin components. The albumin is the smaller molecule, and is said to exert about four times as much osmotic pressure as the globulin. The albumin/globulin ratio taken alone has no particular significance—it may be low because of increased globulin and a serum in which the albumin is decreased and the globulin normal or raised may therefore exert a lower osmotic pressure than a serum of equal or less total protein content but containing a higher proportion of albumin. From the Tables given in the paper it would seem that oedema in tropical macrocytic anaemia is not explicable solely on a basis of low serum protein.

Although the response to treatment was slow the average duration being 105 days, the majority of patients were ultimately returned to duty in Category A. Treatment consisted of a daily diet of about 4 000 calories, containing 165 gm. protein of which 38 gm. was derived from meat (muscle) 22 gm. from liver 31 gm. from milk, and 12 gm. from eggs. In addition, each patient received 2 to 4 oz. of a marmite substitute vitamin tablets iron and sometimes 2 oz. of yeast. Some also received liver extract orally or by injection. In only two so treated was a reticulocyte response observed. Two patients showed a reticulocyte response to the marmite substitute. Eight patients had one or more blood transfusions because of their precarious condition, while five of the oedematous patients received intravenous infusions of reconstituted serum. This latter treatment was followed by diuresis and in three cases the oedema and ascites began to clear up a few days later. In the other two it seemed to have little effect. In cases with effusions not causing serious mechanical embarrassment, paracentesis was considered undesirable because it involves loss of protein to the body.

The method used for serum protein determination was based on that of WALTHER (*Lancet* 1941 Sept. 20 337) but in the absence of a colorimeter a Lovibond tintometer with a blood urea disk was used. The serum non protein nitrogen estimations were not entirely satisfactory the colour comparison often being hindered by cloudiness but fortunately the protein equivalent of the N.P.N. is small and the inaccuracy involved not material when the N.P.N. is high the difficulty disappears since greater dilutions can be used. Fractionation of the albumin and globulin was carried out on the usual principles with sodium sulphate. In the absence of suitable filter paper the clear supernatant solution was pipetted off after standing. *F Murgatroyd*

ROSENBAUM S Chronic Leucopenia in Childhood *Harefuah* Jerusalem  
1945 Oct 15 v 29 No 8 [In Hebrew 188-91 English summary 191]

Chronic leucopenia (5 500 and fewer leucocytes per cmm) was found in 13 per cent of 880 children. Chronic decided leucopenia (50% and less of the normal leucocyte values for the corresponding age) was found in 3% chronic lymphocytopenia (50% and less of the normal lymphocyte counts for the corresponding age) in 1 7%.

62 5% of these children were underweight.

Chronic leucopenia may be either congenital or acquired. Familial cases were observed.

The condition may continue for years.

In one third of the cases there was an eosinopenia. But considerable eosinophilia may be observed. The eosinophilic system reacts by itself independent of the granulocytic or lymphocytic system.

The percentage of eosinophiles not the total eosinophile count is characteristic of an allergic reaction.

Chronic leucopenia is in the vast majority of the cases a sign accompanying a transient or permanent inferiority of one or more functional systems. These children suffer from catarrhal diathesis, muscular weakness, neuropathic and psychopathic conditions, and allergic affections are also relatively frequent. Nutritional disturbances due to digestive insufficiency and lambliosis may produce chronic leucopenia. In two cases premature birth may have been the cause.

Chronic decided leucopenia and chronic lymphocytopenia correspond in their pathognostic significance entirely to chronic leucopenia. In febrile infections there is an increase in the white blood cells. But this increase is relatively moderate. The children react within the limits of their diminished leucocytic reactive power. In purulent conditions the granulocytes are chiefly increased in catarrhal infections, chiefly the lymphocytes.

The sulfonamide drugs and salicylic acid do not seem to be a special danger in the sense of agranulocytosis. Nor have spontaneous agranulocytoses been noted.

WEINGARTEN R J Influence of Temperature on Sedimentation-Rate Its  
Clinical Significance *Lancet* 1945 Oct 27 526-8 3 figs

The influence of temperature on erythrocyte sedimentation rate was investigated because experience suggested that the common belief that high external temperatures accelerate and low temperatures retard the rate was false. In the investigation the Westergren method was used with all technical precautions. Readings were taken every ten minutes, blood was withdrawn with as little venous stasis as possible, the patients having been kept fasting. Comparative determinations were made at 99°F and at 44°F. Preliminary experiments showed that previous chilling or warming of the specimens did not materially influence the rate in the actual determinations.

Of 483 miscellaneous cases examined 279 (57 7 per cent.) showed a higher sedimentation rate at 99°F. 109 (22 7 per cent.) showed a higher rate at 44°F and 95 (19 7 per cent.) showed less than 10 per cent. difference between the rates at the two temperatures at any stage during an hour. Thus the general statement that erythrocyte sedimentation rates are raised at higher temperatures is not correct.

In patients with hepatic disorders an increase in sedimentation rate at low temperatures was most pronounced, readings in the first 10 minutes often being more than five times as high in the cold as in the warm environment. In the

cold, the fall of the corpuscles was very rapid during the first 30 minutes slowing down only as packing prevailed. In all these cases the clumping of the erythrocytes into large visible aggregates was remarkable occurring usually a few minutes after the tubes had been placed in the cold. This phenomenon was very pronounced in a case of blackwater fever sedimentation being complete in under two minutes.

F Margatroyd

## VENOMS AND ANTIVENENES

BOQUET P. Sur les propriétés antivenimeuses du sérum de *Vipera aspis* [The Antivenene Properties of the Serum of *Vipera aspis*] *Ann Inst Pasteur* 1945 Sept.-Oct. v 71 Nos. 9-10 340-43

The blood of the common viper of France is toxic but the symptoms it produces are not the same as those set up by the venom. The venom is a blood-coagulant and contains a phosphatidase enzyme capable of transforming lecithin into haemolytic lysocithin. The serum is haemolytic owing to its direct action on the red corpuscles and is not a coagulant and the toxicity of the serum is not affected by antivenene. Again, the serum when heated to 55°C. loses its toxicity but neutralizes the venom as strongly as the best antivenenes prepared by a long course of immunization of horses. It also neutralizes at least to some degree, the venoms of other Viperidae *Bilis aridans* *Cerastes cornutus* *V. russelli* and *Bothrops atrox*.

Venom and antivenene combine to form an insoluble product but the admixture of serum and antivenene does not result in any precipitation. Nevertheless the neutralizing property of the viper serum is derived from the venom. It is thought that a small part of the venom, in the course of its elaboration in the parotid, gains entrance to the blood like an internal secretion. This is at variance with the idea that a substance can be antigenic only if it is foreign to the organism.

H Harold Scott

DEL POLO E C GONZÁLEZ Q J & MEXERES T H. Acciones del veneno de alacran sobre el aparato respiratorio [The Action of Scorpion Venom on the Respiratory Apparatus.] *Rev Inst Salubridad y Enfermedades Trop* Mexico. 1945 June, v 6 No 2, 77-84, 4 pls. English summary

SERGEANT Et. Sérothérapie antiscorpionique (Huitième note). Observations médicales reçues pendant l'année 1944 [Anti-Scorpionic Serotherapy Eighth Note 1944.] *Arch Inst Pasteur d'Algérie*. 1945 June v 23 No. 2, 111-14

Since 1936 of 1 739 cases of scorpion sting reported, 470 were regarded as dangerous to life and were treated with serum. The percentage of recovery was 89.3 (420 subjects) [See this Bulletin 1945 v 42, 404]

KIRBY SMITH H. T. Specific Treatment of Black Widow Spider Bites. *Southern Med J* 1945 Oct. v 38, No 10 696-8.

"It is the conclusion of the writer that the treatment of black widow spider bite with black widow spider antivenum administered a comparatively short time after the bite is successful in relieving pain and preventing its recurrence."

## DERMATOLOGY AND FUNGUS DISEASES

BAGBY J W A Tropical Lichen Planus-Like Disease *Arch Dermat & Syph*  
1945 July v 52 No 1 1-5 6 figs

The author states that since the beginning of the war numerous cases of a disease which in its clinical appearance is suggestive of lichen planus have been noted on some tropical islands of the Pacific. In some instances the disease begins as true lichen planus in others as a generalized erythematous exfoliating eruption the efflorescence of the primary lesions being followed by the appearance of localized lichenoid papules. A third group is described in which the primary lesions are bullae which are replaced by papules or nodules simulating hypertrophic lichen planus. Usually the distribution is generalized but in several cases the mid portion of the trunk has been free from lesions. The face scalp palms and soles may be involved also the tongue and buccal mucosae. As the eruption retrogresses pigmentation of the affected areas is noted in some instances the residual lesions are atrophic depressed deeply pigmented scars.

The clinical histories of five cases are recorded and details and illustrations of the results of histological examinations are given. All the patients were white men all except one—who was 27 years old—were aged from 42 to 47. Their period of tropical service had varied from 2 to 19 months. All except one had taken 0.1 gm. of quinacrine hydrochloride (mepacrine) daily the exception had received this drug and quinine [doses not stated] for an attack of malignant tertian malaria which had subsided seven days before the eruption appeared. Most of the men had lost weight before the lichen developed. The author notes that the eruption tends to improve when the patient is en route to the United States he has not seen the malady in negroes. He adds the following comments:

1 Several men with lichen planus were seen in the eastern part of the Solomon Islands in 1943 but none with this atypical form was observed. Many more cases of this eruption have appeared in 1944 than in 1943 though the administration of quinacrine hydrochloride and the dietary allotments were the same for both years.

2 Various forms of lichen planus had been observed long before quinacrine hydrochloride came into use.

3 I have administered quinacrine hydrochloride to five men nearly well of the disease giving each three tablets daily for four days (admittedly a short trial) without causing a flareup of their lesions.

4 The eruption has none of the features usually associated with dietary deficiencies or with drug eruptions.

5 The disease has appeared in men who had been in the tropics for only two or three months in which period it is not likely that severe avitaminosis would occur.

[This paper is important as it is believed to be the first which has been published concerning a malady that has attracted the attention of military dermatologists and malarologists serving in sub-tropical and tropical areas. Medical Officers serving with the British Forces have only recently been permitted to submit their observations on this disease for publication. It will be noted that whilst the author indicated that quinacrine hydrochloride is a common factor in all cases he does not attribute the eruption solely to this cause. Those interested in the matter may care to trace the following references: *Arch Dermat & Syph.* 1944 v 49 224 and 1945 v 51 353 also *Lancet* 1945 Dec. 1 711.]

R M B MacKenna

BERGER L. BEADRY M & GAUMOND E. Chromoblastomycosis due to a New Species of Fungus (First Canadian Case) *Canadian Med Ass J* 1945 Aug 1 53 No 2, 138-42, 6 figs. [10 refs.]

The authors give a careful survey of the history of chromomycosis and describe a new case—the first example of the disease recorded in Canada.

The lesion of chromomycosis generally affects only one region—in 90 per cent. of cases it is on the lower extremity because of its greater exposure to trauma. In the Canadian case however the lesions were multiple and widely distributed. The granuloma appeared first on the web between the 4th and 5th fingers of the left hand and on reaching the size of a hazel-nut, it was excised after an erroneous diagnosis of prickle-cell carcinoma. A month later it reappeared and spread all over the dorsum of the left hand, while secondary granulomata appeared on the left forearm the right hand, the left foot the buttocks the right cheek and the right ear. The lesions consisted of thick warty cauliflower-like masses of pink, brown or violet colour with a more or less moist surface from the continual oozing of a foul-smelling exudate. Histologically the granuloma did not differ essentially from that seen in typical chromomycosis but the yeast-like form of the parasite in the tissues was relatively small, usually thin-walled and showed budding forms and chains of cells whereas the common fungi of chromomycosis (*Phialophora verrucosa* and *Hormodendrum pedrosoi*) appear in the lesion as thick walled cells often septate but never budding. In culture the fungus from the Canadian case grew freely on the common media used in mycology as brown or black yeast-like colonies of creamy consistency. The macroscopic morphology of the fungus in culture presented the characters of the genus *Candida* but because of its black colour EMMONS and CARRION considered it to be related to *Pullularia pullulans* (syn. *Dematiium pullulans*). The authors are, however, contented for the present to consider the strain as 'a black *Candida* like but still unnamed new species.

Treatment consisting of intensive iodine and X-ray therapy autovaccination with the fungus and local injections of arsenic and methylene blue was without avail. After two years of fruitless chemotherapy the lesions were removed by amputation electrocoagulation and scraping. The subsequent history of the case is not yet available.

J T Duncan

LEVY B M. Chemotherapy of Experimental Histoplasmosis in White Mice. *Amer J Trop Med* 1945 May 5 25 No 3 241-51 8 figs. [47 refs.]

Up to the present time no drug treatment has been found effective in histoplasmosis—the following have been used without success—Fuadin Neostam sodium iodide neosarphenamine bismuth pentnucleotide and liver extract sulphanilamide sulphathiazole sulphapyridine atabrine [mepacrine] Pronitryl, potassium arsenite quinine, cinetine Sulpharsenal, vitamins and other remedies.

As apparently no chemotherapeutic experiments had been made on artificially infected animals the author undertook this work and, using a freshly isolated strain of *Histoplasma capsulatum* he inoculated, intravenously 145 young white mice with the living culture. The inoculum was prepared by grinding up and suspending in sterile isotonic saline a seven-days-old culture on blood-agar at 37°C. consisting of the mixed mycelial and yeast forms of the fungus. The density of the suspension was adjusted to equal that of

No. 4 McFarland barium sulphate standard, and the infecting dose used for intravenous injection was 0.2 cc. Within 24 hours of inoculation treatment was started by injecting, by the peritoneal route appropriate doses of the following drugs in sterile solution—sodium iodide Neostam, Fuadin

sulphanilamide proflavin thymol B-9 (an organic iodide) and sodium propionate. All the animals in the eight groups developed histoplasmosis and in no case had the drug any observed effect on the course of the disease.

J T Duncan

DA SILVA LACAZ C Contribución brasileña para el estudio de la blastomicosis sud americana (Granulomatosis paracoccidioidesca) [Brazilian Contribution to the Study of Paracoccidioides Granuloma] *Arch Uruguaya de Med. Cirug y Especialidades* 1945 Aug v 27 No 2, 167-81 English summary

## HEAT STROKE AND ALLIED CONDITIONS

BORDEN D L WADDILL J F & GRIER G S III Statistical Study of 265 Cases of Heat Disease. *J Amer Med Ass* 1945 Aug 25 v 128 No 17 1200-205 8 figs. [13 refs.]

This is an incomplete study of heat casualties occurring among troops undergoing training in a southern coastal area of the United States. In the summer of 1942 there were four fatal cases of heat stroke. In May to September 1943 265 cases of effects of heat (heat disease) were admitted to hospital [the total population at risk is not stated] there were three fatalities. For statistical purposes the cases seen in 1943 were divided into two main groups—mild and severe but the proportion of the one to the other is not reported. An analysis of cases according to age amount of training and home State southern or northern is given but the corresponding distribution of the total population is not stated. For treatment the division was into group 1—cases without circulatory failure and with cramps and group 2—cases with circulatory failure. The former group is labelled by the authors Heat Prostration and apparently about 14 per cent of all the cases came under this category. The second and larger group were all regarded as exhibiting different degrees of the same pathological process. The milder cases showed mainly circulatory collapse and were called heat exhaustion. The more severe cases showed hyperthermia and were called heat stroke [it is not obvious that any real flash hyperpyrexias or heat strokes were seen though the history of one of the fatal cases is suggestive]. Nearly all cases showed some pyrexia.

The treatment of the group 1 patients was by rest and sedatives cooling by water spray and by fan water and salt orally in all cases and intravenous saline in severe cases. 0.9 per cent saline intravenously was found to be specific for the relief of cramps. In the group 2 patients who showed evidence of shock plasma transfusions were given rather than saline to avoid the danger of pulmonary oedema pure oxygen was given in all severe cases. Patients with definite hyperthermia were cooled by spraying and ice bags. All cases of effects of heat were considered to be emergencies and the patients were taken to a special treatment room immediately on admission, and later transferred to an air-conditioned recovery ward. [The Americans here are following the practice adopted by the British Army in Iraq in 1941 of having special heat stroke centres in all hospitals equipped with air conditioning and of having air-conditioned wards available for heat and other cases.] Pathological findings are not reported in detail here but are promised later. Post-mortem findings on three fatal cases in 1943 showed widespread petechial haemorrhages in brain intestine lungs and blood vessel endothelium and passive congestion in liver and lungs [similar findings have often been reported before].



The authors consider that all "heat disease" is due to heat accumulation resulting from inadequate evaporation when heat losses from convection, radiation and conduction are minimal owing to a high dry bulb temperature. They therefore believe that the wet bulb temperature is a good indicator of the probable incidence of heat disease, particularly at low wind velocities. They show charts correlating wet and dry bulb temperature and heat cases over the three hottest months of the year in support of this view. Accordingly in 1943 the physical activities of the troops in this area were limited on hot humid days and close order drill and severe training were stopped when the dry bulb temperature was 88°F or over and the wet bulb 77°F when the wind velocity was above 10 miles per hour or—if the wind velocity was below 10 miles per hour—when the wet bulb thermometer was 75°F or over. It is not stated whether this measure gave a reduced instance of heat casualties as compared with that in 1942. The troops were advised to drink 500 cc. of 0.1 per cent. saline each hour while at exercise in the heat and patients with heat exhaustion who gave a history of not taking the prescribed amount of salt were subjected to appropriate disciplinary action.

[This is a useful study but unfortunately it does not go into sufficient detail. The statistical information is inadequate and the account of the symptomatology is very compressed, e.g. there is no indication of the degree of pyrexia in the various cases other than that their temperatures were above 99.6°F. The association of symptoms is not considered at all. The promised pathological report should, however, be interesting.]

W. S. S. Ladell

BROWN H. F. The Physiological Effects of Sunlight on Man. *Physiol. Rev.* 1943 July v 23 No 3 483-530 4 figs. [281 refs.]

The author's thesis is that all the evidence points to the physiological effects of sunlight on man being detrimental rather than beneficial. With the exception of the effect on avitaminosis D sunlight and even ultra-violet light is probably nothing more than a good placebo.

The spectral distribution of sunlight is from wavelengths less than 0.3 $\mu$  to beyond 2  $\mu$ . The distribution is affected by passage through the atmosphere—the ultra violet in particular is absorbed by ozone and small dust particles, hence there is most ultra violet all the year round in the tropics where the ozone is least and little ultra violet in the winter in temperate regions because the air mass is then greater and there is more ozone. The visible spectrum is not much affected by these factors, hence it may seem to the eye to be as bright at 5 p.m. as earlier in the day but sunburning which is due to the ultra-violet will not occur owing to the greater air mass through which the radiation passes. Similarly a fine dust haze will screen off the ultra violet without any visible diminution in intensity. On the other hand, diffusion by dust and water droplets gives rise to sky radiation which is rich in ultra violet light so sunburning will occur on an apparently overcast day.

On reaching the skin up to 45 per cent. of the total sunlight is reflected if the skin is white but only 16 per cent. if it is black—the major portion of the rest is absorbed before it has penetrated more than a few millimetres. The maximum penetration is with wavelengths between 0.7 and 1.5 $\mu$ . HARDY found only 8 per cent. transmission of infra red radiation through two millimetres of human skin. With wavelengths below 0.32 $\mu$  transmission is also very low—the radiation is scattered by dead cells in the corneum and absorbed by the protein of the cells so none is transmitted and not much reflected. Radiation of wavelengths of 0.5 $\mu$  is not absorbed in the corneum—some is reflected and some gets through to the blood vessels beneath, where it is absorbed by the haemoglobin. Wavelengths of 0.6 $\mu$  are not absorbed by

haemoglobin and get through to subcutaneous tissues. Longer wavelengths than are found in the sun's radiation are all absorbed superficially. In the eye maximum transmission is of radiation at wavelengths  $0.8\mu$  in general penetration is deeper and there is no scatter. The ultra violet is absorbed by the protein in the coats and media and in the infra red there is zero transmission with wavelengths  $1.4\mu$  owing to absorption by the water of the aqueous and vitreous but enough infra red can get through to the retina to cause burns—eclipse blindness. It is dangerous to look at the sun through glasses which filter off visible radiation only. The retinal pigment absorbs all radiation that reaches it.

Most of the radiation is absorbed non-specifically and heats the skin. Sunlight gives rise only to thermal sensations the greatest intensity of sunlight ( $0.03 \text{ gm. cal cm}^2 \text{ sec}^{-1}$ ) is not sufficient to give rise to pain. The stimulus for thermal sensation is an alteration in the temperature gradient in the skin hence the infra-red which is absorbed superficially gives the best effect so radiation from a hot stove is a more effective stimulus than sunlight. Negroes, whose skins are better absorbers of sunlight have a lower sensory threshold to it than have whites. The radiant energy absorbed on the skin may raise the surface skin temperature above the body temperature especially if the circulation to the skin is diminished or stopped so that distribution of the heat to the rest of the body by the blood-stream cannot occur. The solar heat load on a naked body may be large and equal to the metabolic heat load of walking at 3 miles per hour. It is more for negroes whose skin does not reflect so much of the sun's radiation but in all cases it can be reduced by clothes. It does not vary much with latitude as there is only 20 per cent difference in intensity of the total radiant energy from the sun between the sun at zenith and the sun at  $60^\circ$  from zenith.

The chief photo-chemical effect of sunlight is sunburn. After about half an hour's exposure to sunlight (the exact threshold for intensity and for time varies greatly between individuals and at different times) there is a latent period after which erythema and a slight swelling develop. With longer exposures there is marked oedema followed by desquamation and blistering. Later the erythema gives place to tanning and finally the sun tan itself darkens with further exposure. The erythema is produced solely by rays of shorter wavelength than  $0.32\mu$  i.e. by ultra violet light. The time the erythema takes to develop varies with different wavelengths. No histological changes are found before the erythema appears. Blum considers that the first action of the ultra violet is on the cells of the Malpighian layer. Comparison between the action spectrum and the respective absorption spectra indicates either cell protein or nucleic acid as the light absorber. Blum favours the protein. There are some discrepancies explained. The ultra violet light produces in the cells a dilator substance which differs somewhat from the H substance. MENKIN (*J Exper Med* 1936 v 64 485) has called this leucotaxin. This substance diffuses down to the papillary vessels hence the latent period between exposure and erythema. Leucotaxin increases capillary permeability causing oedema and exerts a chemotactic effect stimulating the migration of leucocytes out of the vessels. This hypothesis is supported by the finding of an increased concentration of dilator substance in the skin and blood of animals after ultra violet radiation. The cells of the epidermis degenerate either owing to a direct effect of the ultra violet or according to Menkin (*Arch Pathology* 1943 v 36 269) as the result of the production of another substance necrosin. The longer wavelengths of the erythema spectrum may also penetrate far enough to have a direct effect on the papillary vessels. There is not yet any explanation of the continuation of the erythema for a long period without further exposures.

The erythema is replaced by sun tan. The sun-tan spectrum is the same as the erythema spectrum. First there is a migration of melanin granules from the basal cells to more superficial layers and then there is formation of fresh melanin in the melanoblasts. Though melanin can be formed *in vitro* by the action of ultraviolet light in the presence of ferrous salts on tyrosine this process requires more ultra-violet than can reach the basal cells in sunlight and cannot take place without free oxygen, whilst sun-tanning can occur in skin deprived of oxygen. Bloem (*Zischer Physiol. Chem.*, 1916 v. 98 228 *Amer. J. Med. Sci.* 1929 v. 177 608) however finds dopa-oxidase in cells injured by ultra violet light and suggests that melanin is formed in them from L-dopa (laevorotatory  $\beta$ -3-4-dioxyphenylalanine) brought to them by the blood stream.

After the sun-tan has developed, radiations of wavelength up to  $0.42\mu$  cause a further darkening of the tan without formation of more melanin. This darkening occurs more rapidly than the initial tanning and may be due to oxidation of a reduced leuco-melanin as it will not occur in the absence of oxygen. This longer wavelength radiation is not stopped by glass and is also present in winter sunlight hence the retention of sun tan by some individuals throughout the winter. A similar darkening of pre-formed melanin can be brought about by the administration of sex hormones.

A sun-tanned skin gives some protection against sunburn this is due primarily to a hyperplasia of the cells of the corneum after ultra violet irradiation, and the thick layer of cells that results shields the sensitive basal layer from further irradiation. When the corneum regains its original thickness most of the immunity passes off though the sun tan remains. There is, however, some protection from absorption of the ultra violet light by the melanin which has migrated superficially this is the cause of the relative immunity of negroes to sunburn. In addition there is some cellular immunity to the action of ultra violet light which develops 12 hours after exposure. Sweat and sebum have no effect on the erythema threshold, but artificial protection against sunburn will be given by any substance that absorbs the wavelengths concerned, i.e. from  $0.29$  to  $0.32\mu$ .

The belief that exposure to sunlight can cause tumours comes from the observed greater incidence of cutaneous cancer among outdoor workers and on areas of exposed skin. This belief is supported by the observation that malignant tumours develop in rats and mice after ultra violet irradiation. The carcinogenic rays are of the same wavelengths as the erythema rays. The action of the ultra violet light is either direct injury of the cells or the induction of somatic mutations by its action on nucleic acid. There is a discrepancy in that in mice the tumours are sarcomata whereas in man they are carcinomata. This is explained by the thickness of human skin which is so great that the radiation cannot penetrate to the connective tissue beneath. Cutaneous cancer is certainly more common according to Dorn (*Pub. Health Rep. Wash.* 1944 v. 49 pp. 33 65 and 97) in latitudes where there is more ultra-violet thus at  $41^\circ$  the incidence in the United States of America is 23.1 per 100,000 but 9 further south it is 116.4.

The action of the ultra-violet radiation on certain steroid compounds to provide vitamin D in the skin takes place in the corneum, and considerable amounts of the vitamin may be lost in desquamating cells after irradiation. The release of leucotaxin or of some vasodilator substance is probably the cause of a fall in systemic blood pressure observed after sunburn and after irradiation from a carbon arc, which has a similar spectrum to sunlight. No direct effect of sunlight on metabolism and growth has been found. The sexual cycle of certain animals is affected by light probably because, with longer illumination, waking hours are longer and there is greater activity. Cook (*New*

York J Gynec & Obstet 1894 v 4 282) described suppression of menstruation in Esquimaux women during the dark Arctic winter but this has not been confirmed.

Excessive sunlight on the eyes causes photo-ophthalmia this is simply sunburn of the eyes. Very long wavelength radiation will produce cataract (glass blowers cataract) and also intense ultra violet irradiation of the lens might injure it and give rise to opacities but the high incidence of senile cataract in countries near the equator is probably not due to insolation.

Certain dyes and naturally occurring pigments have a photo-dynamic action when introduced into living systems they render the cells photo-sensitive so that oxidative processes usually injurious take place on exposure to light. Porphyrin pigments are photo-dynamic and as they may be derived from plants, grazing animals are sometimes affected, and this may be of great economic importance in some regions but man is rarely directly affected in this way.

Though sunlight is a major factor in man's environment it is not so by direct physiological action. It is easy to escape from a solar heat load by shade and suitable clothing and it is possible to avoid sunburn by simple precautions. The rôle of the sun in heat disease is thermal only there is no specific sun stroke effect. The biological success of the negro in the tropics cannot be attributed to his pigmentation because of the pigment the negro absorbs more solar radiation and has a greater total heat load than the white man under similar conditions he is however less sensitive to sunburn.

W S S Ladell

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## MISCELLANEOUS DISEASES

HYMAN A S Heart Disease in the Jungles of the South Pacific some Observations made among Melanesians of the New Hebrides and Solomons Islands Area. *Ann Intern Med* 1945 May v 22 No 5 630-52

The author who is well known as a cardiologist took advantage of an opportunity of examining Melanesian labour recruits to study cardiac disturbances among them and has written a paper of much interest. He found the incidence of arteriosclerosis to be unduly high as compared with European and American subjects. The men seemed to be old at fifty and in many over 30 years of age tortuous temporal arteries were observed and radials were thickened. Blood pressure varied in a peculiar way in different localities in some the levels were low 80-90 mm. Hg systolic and 40-50 diastolic but in three islands [they are not specified] high readings up to 236 mm. systolic and 115 diastolic were observed in one tribe 11 out of 19 persons over 30 years of age had high pressures and one boy of 18 years gave readings of 160 and 104 respectively. Six out of nine with high pressure gave a history of previous blackwater fever and among the Native Medical Practitioners—a shrewd body of men—there is a current belief that blackwater fever is often followed by hypertension. Cardiac hypertrophy was another common finding for which no cause could be discovered.

Sinus arrhythmia and extra systoles were fairly frequently met with of murmurs the commonest were pulmonary systolic functional in nature and next apical systolic also classed as functional as no concomitant signs of heart disease were discovered. This may have been syphilitic in nature but was not so determined. Chronic coronary disease is common but often unassociated with pain, and even when there is pain it is comparatively slight and bears no resemblance to the acute angina pectoris of Europeans. Examination to

compare the pain threshold of the native with that of the white man revealed no difference in degree. Pain and oedema of the feet are found associated with vascular occlusion of the vessels of the leg and foot, which in turn are thought to be due to infections of the limb sustained in the jungle varicose veins are commonly seen, even in children, and "may have been due to secondary changes the result of continuous re-infection of the feet by various tropical organisms. [This is purely speculative and calls for further research, as indeed does the whole subject of cardiovascular disease among natives, and it is of particular interest in this region of the South Pacific where such lesions are common in one island but are rarely seen in others close by]

H Harold Scott.

SANABRIA, A. & PLANCHART M., A. El factor carencial en la cirrosis hepática y en la miocarditis bilharziana. [The Deficiency Factor in Cirrhosis of the Liver and in Bilharzial Myocarditis.] *Rev Policlínica Caracas*. 1945 May-June, v 14 No. 82, 163-97 1 chart & 19 figs. [78 refs.] English summary (7 lines)

The authors start with a statement and consideration of the many reputed causes of hepatic cirrhosis which have been brought forward from time to time (race, sex, heredity alcohol, nutritional and toxic causes etc.) with quotations from the literature of those who have suggested and supported these various theories. They conclude from all this that in hepatic cirrhosis nutritional deficiency plays an important part and that this deficiency is probably specific. They point out that cysteine and methionine exert a powerful action in the production of healthy liver cells and in preventing necrosis also that fatty infiltration of the organ is an important precursor of cirrhosis and that choline serves to prevent this. Elsewhere it is stated that cysteine is harmful to the liver and may produce irregular proliferation, but that cysteine which in other circumstances provokes necrotic lesions of the liver is beneficial in the presence of choline inasmuch as the methyl groups resulting from the cysteine and the choline bring about the transformation of it into methionine. Hence the benefit which has been reported in cirrhotic patients from the use of choline chloride, with its lipotropic action.

Again, thiamin plays an active part only when it is converted into diphosphothiamin and patients with hepatic cirrhosis excrete much larger quantities of thiamin than do normal persons.

Six cases are mentioned and a few details on each are given. Three [perhaps four] had ascites and four enlargement of the liver (in another the liver could not be palpated owing to the tenseness of the abdomen) four were passing ova of *Sch. mansoni* one had dysentery and two had positive Kahn reactions.

Benefit was reported in all from treatment with a diet of high protein liver extract choline chloride and mercurial diuretics together with a combination of vitamins A B and D. [An elaborate scheme is presented in which more than a score of arrows point to chronic deficiency of vitamins, and there are several photographs of patients overexposed (in all senses of the term) so that they convey little information. The whole article to the abstracter at least, savours rather of special pleading and is not very convincing especially as so much is based on so small a number of cases.]

H Harold Scott.

MAYER, J H Chronic Melioidosis. A Case showing Multiple Lesions of Bones, Joints, and Lungs. *J Bone & Joint Surgery* 1945 July v 27 No 3 479-85 5 figs. [14 refs.]

This paper describes a case of melioidosis which is of particular interest in that it is the second to be reported in a European—a British soldier—and that

it ran a chronic course the majority end fatally in a few days or weeks. This case has already been reported by MAYER and FINLAYSON [this *Bulletin* 1944 v 41 694] The present account adds little to what has already been published  
S P Bedson

ÖZTURA M H Ueber einen Fall von Morbus Behçet [A Case of Behçet's Syndrome.] *Ophthalmologica* 1944 Dec. v 103 No 6 288-92.

The patient a man aged 38 was under observation at a hospital in Istanbul from June to October 1943 he gave a history of having had recurrent attacks of the syndrome during the preceding four years At the hospital he was examined clinically by doctors of several special departments and various laboratory tests were made.

The symptoms were typical of the disease except that only one eye—the right—was involved the left remaining unaffected throughout the course of the disease

Cerebrospinal fluid was injected into two rabbits and three guineapigs, into the anterior chamber of the eye into the conjunctiva intravenously and intraperitoneally with negative results

Treatment with vitamins B<sub>1</sub> and C and sulphonamides had no effect

No cause was found virus-like elementary bodies have repeatedly been seen in Giemsa-stained smears of the aphthae in the mouth The diagnosis is made difficult by the fact that the three chief symptoms—aphthous ulceration in the mouth ulceration of the external genital organs, and the eye lesions (conjunctivitis corneal opacity hypopyon hyphaemia glaucoma) do not appear simultaneously but in irregular order in different cases. [See also this *Bulletin* 1944 v 41 780]  
J F Corson

VAUGHN A M, HOWSER J W & SHROPSHEAR G Alnham (Dactylolysis Spontanea) Report of Two Cases from Illinois. *Ann Surgery* 1945 Nov v 122, No 5 868-77 8 figs. [10 refs.]

BERKOWITZ S Caterpillar Dermatitis. *Bull U.S Army Med Dept* 1945 Oct v 4 No 4 464-7

A species of caterpillar was found to be the cause of attacks of urticaria among the troops in New Guinea which sometimes almost reached epidemic proportions It occurred again in Northern Australia and was investigated. The caterpillars were allowed to crawl on the arms of 15 volunteers some developed local urticaria within a few minutes and this was replaced after 3 or 4 hours by a pruritic papular eruption which lasted for several days. Others had a discrete papular eruption which appeared after 6 hours and lasted for a few days to a week or longer Similar reactions were produced by rubbing the skin with the cocoons or the tuft of hairs at the tail of the female moth. When extracts of the caterpillars were placed on the skin no reaction occurred unless the skin was scarified, and patch tests with filtrates of extracts were negative. Caterpillar hairs soaked in various liquids for 24 hours still caused reactions as did baked hairs also but not hairs which had been pounded in a mortar

It was found from these experiments that the dermatitis is produced by the inoculation by means of barbed hairs of an unknown irritant The Australian caterpillar concerned is *Ochrogaster contraria* the name of the New Guinea caterpillar is not given. [See also this *Bulletin* 1923 v 20 801 1933 v 30 317 1936 v 33 489]  
J F Corson.

## GENERAL PROTOZOOLOGY

KISKADDON R. M. & REMSHAW R. J. F. Human Coccidiosis. *J Amer Med. Ass.* 1945 July 7 v 128 No. 10 731-2, 1 fig

In the stools of a man aged 60 suffering from ulcerative colitis, certain double-contoured cysts, measuring on an average  $10 \times 7$  microns were discovered. The contents of the cysts were a granular protoplasmic material which showed no signs of further development though observed for months. The authors refer to the structures, one of which is shown in a microphotograph as cysts of *Isospora hominis*. (It is possible that they are undeveloped sporozoites of this parasite, but without evidence of their further development it is not justifiable to make even a diagnosis of coccidiosis much less one of *I. hominis*.) C. M. Weyon.

KEAM B. H., & GROCOTT R. G. Sarcosporidiosis or Toxoplasmosis in Man and Guinea-Pig. *Amer J Path.* 1945 May v 21 No 3 467-83 5 figs. on 2 pls. [41 refs.]

Cases of sarcosporidiosis in man fall into two groups. The first comprises those in which the parasite is large and enclosed by a striated capsule. The relatively large sporozoites are in groups separated from one another by septa. The characters are those of such well known sarcosporidia of animals as *Sarcocystis tenella* and *S. mieschkeana*. The second group includes those in which the parasite is smaller while the limiting membrane is thin and not striated. The sporozoites are smaller than those of the parasites of the first type and are not separated into groups by septa. The first case in which the parasite was of the second type was one discovered by Darling in 1909 in Panama. He realized that the parasite differed from the typical sarcosporidia but attributed the differences to the influence of an unusual host which man was considered to be. He fed guinea-pigs on infected mouse tissues and subsequently found similar modified parasites in these animals. The present paper describes the case of a woman in whom parasites of the second type were found in the heart muscle, and also records the discovery of similar forms in guinea-pigs which had not been subjected to experiment. It is concluded by the authors that in Darling's experiments the natural occurrence of parasites in his experimental guinea-pigs had not been excluded, so that it is more than doubtful that the parasites seen in the guinea-pigs represented modified mouse parasites. In the guinea-pigs parasites were found by the authors in the brain and kidneys as well as in the muscles. It is concluded that the cases in which the parasites are of the second type are more probably instances of toxoplasmosis than of sarcosporidiosis. In the absence of serological and inoculation experiments a final classification of the parasites cannot yet be made. C. M. Weyon.

## GENERAL ENTOMOLOGY

MADDEN A. H. LINDQUIST A. W. & KNIPPLING E. F. DDT Treatment of Airplanes to prevent Introduction of Noxious Insects. *J Econom. Entom.* 1945 Apr v 38 No. 2, 252-4

Tests were made in the laboratory in an artificial cage resembling a part of an aircraft and in aircraft themselves, of the value of DDT as a residual insecticide. Four types of application were used—acrosols combined with

pyrethrum dusts wet sprays and fine mist sprays—and evaluation of the treatments was made at intervals up to nine weeks by exposing mosquitoes and houseflies in treated airplanes for  $1\frac{1}{2}$  to 2 hours and counting the insects that were down

A much more prolonged effect was seen in aircraft with upholstered interiors than in those with an all metal finish when aerosols and dusts were used [no comparative data are given for wet and fine mist sprays] In upholstered aircraft the knock-down with different applications was —

Aerosol ( four or five times the recommended dosage ) 42 per cent. after 3 weeks.

Dust (average dose 2 oz.) 100 per cent. after 6 weeks.

Wet sprays 5 per cent. DDT (300 ml. for an average fighter plane) 80 per cent after 6 weeks.

Fine mist sprays 20 per cent. DDT (23 to 35 ml. per plane) practically none after 3 weeks

Fine mist sprays 20 per cent DDT (400 ml. per plane) complete knockdown after 12 days.

The authors conclude that DDT is a useful adjuvant to normal spraying which it should greatly reinforce but not replace G Macdonald

LINDQUIST A W TRAVIS B V MADDEN A H SCHROEDER H O & JONES H A DDT and Pyrethrum Aerosols to control Mosquitoes and Houseflies under Semi Practical Conditions. *J Econom Entom* 1945 Apr 38 No 2 255-7

— MADDEN A H WILSON H G & KNIRLING E F DDT as a Residual-Type Treatment for Control of Houseflies *Ibid* 257-61

— WILSON H G SCHROEDER H O & MADDEN A H Effect of Temperatures on Knockdown and Kill of Houseflies exposed to DDT *Ibid* 261-4

Temperature exerts a marked effect on the rate of knock-down and the final mortality of flies exposed to treated surfaces. When exposed at a temperature of 70°F and transferred after being knocked down to a temperature of 80°F to 100°F they recover collapsing again when put back in a cooler climate and again recovering if warmed an alternation which can be repeated several times before death ensues. Similarly the time in which knock-down occurs varies directly with the temperature being more than twice as long at 95°F as it is at 50°F. Flies which had been in contact with a film at a temperature of 70°F never recovered if subsequently held at that temperature but some became active within an hour if they were moved to a temperature of 95°F or 100°F under which conditions the final mortality was usually less than 100 per cent. and this type of relationship between efficacy and temperature was shown to hold good under a variety of circumstances.

A solution of 5 per cent DDT and 5 per cent. cyclohexanone in deodorized kerosene (*Deobase*) gave uniformly better results in terms of knock-down and mortality than a 5 per cent solution in kerosene while solutions in dibutyl phthalate were inferior to those in kerosene.

Solutions and emulsions of DDT applied to screencloth at the rate of 100 mg per sq. ft. gave satisfactory mortality among insects brought into contact with it and did not injure the synthetic screencloth used in U.S. services the effect of emulsions lasted longer than did that of solutions in kerosene or dibutyl phthalate

Tests of the efficacy of DDT on different types of surfaces showed that suspensions had a higher toxicity when applied to inside paint than on unpainted wood and had least effect on full oil or outside paint. Kerosene solutions were relatively ineffective on any painted surface. DDT mixed with



cold water paints, such as calcimine, and applied at the rate of 25 mgm. per sq. ft. gave a slower knockdown than kerosene solutions applied to the surface, but remained effective throughout the test period of 41 days.

In the first paper the authors record the results of an enquiry into the practicability of substituting DDT for pyrethrum in apparatus of the pyrethrum-freon-aerosol type but much of the value of the work is lost as a result of their inability to quote the exact formulae used. DDT was found to be insufficiently soluble in Freon-12 to provide a satisfactory concentration without the use of an auxiliary solvent, for which purpose cyclohexanone was found most suitable. When DDT was used at concentrations 12.5 times as great as used for pyrethrins, the two were equally toxic to mosquitoes. Good results were obtained when they were combined in unstated proportions, and they were improved by the addition of motor oils of various, unstated, viscosities. G. Macdonald

BLAGOVESHCHENSKY D. BRIGETOVA N. & MONCHADSKY A. An Investigation on New Repellents for the Protection of Man against Mosquito Attacks. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945 Oct. 39 No. 2 14-50

This is substantially the same paper as that abstracted in this Bulletin 1944 v. 41 1049

DE MEILLON, B. & LAVOPIERRE M. New Records and Species of Biting Insects from the Ethiopian Region. *J. Entom. Soc. Southern Africa* 1944 v. 7 38-67 5 figs.

An abstract of this paper appears in the *Rev. Applied Entom.* Ser. B 1945 Oct., v. 33, Pt. 10 143

GASCHES H. *Phlébotomes de Suisse*. *Phlébotomes in Switzerland.* *Acta Tropica* Basel. 1945 v. 2 No. 2 137-54 8 figs. 15 refs.

No study of *Phlébotomes* in Switzerland has been published since GALLI VALEIO discovered a specimen of *P. fufus* at Orbe (Aund) in 1912 when this was pointed out by the present author to the Swiss Entomological Society. He received a collection of 21 specimens which were caught at Ascona (Tessin) from June to August 1944.

Two species were identified: *P. fufus* (Newstead 1911) male and female, and *P. parisi* (Adler and Theodor 1927) male only. These are described, with drawings of the genital armatures and wing of the former species and of the genital armature and the buccal armature of the latter. J. F. CORSON.

ARROT L. & MALBRANT R. Notes sur les Phlébotomes. XLVII. Phlébotomes du Moyen Congo. *Arch. Inst. Pasteur d'Algérie* 1945 June 23 No. 2 121-7 4 figs.

PARROT L. MOKNEY J. & C. DEN T. J. Notes sur les Phlébotomes. XLVIII. Phlébotomes de l'Afrique Occidentale Française. I. Senegal, Soudan, Niger. *Arch. Inst. Pasteur d'Algérie* 1945 Sept. 23 No. 3 232-44 5 figs. 32 refs.

### LABORATORY PROCEDURES.

ATCHLEY J., BACON R., CURRAN G. & DAVID K. A Clinical Evaluation of the Copper Sulfate Method for measuring Specific Gravities of Whole Blood and Plasma. *J. Lab. & Clin. Med.* 1945 Oct., v. 30 No. 10 830-33.

A simple method of determining haemoglobin, haematocrit and plasma protein values from the specific gravities of whole blood, plasma or serum with

the help of charts was proposed by PHILLIPS *et al* [see *Bulletin of Hygiene* 1944 v 19 140] The present authors have tested its suitability for hospital practice

The copper sulphate solutions were in 50 cc amounts with specific gravities ranging from 1.008 to 1.075 by differences of 0.002 When 50 drops of plasma were added to these 50 cc amounts the average lowering of the specific gravity was found to be 0.0005

The constancy of the results was tested by determinations by two analysts of specimens of blood from 50 unselected patients in the medical wards the results were sufficiently uniform for clinical work The specific gravity determined by the copper sulphate method was compared with the determinations by the falling drop method of BARBOUR and HAMILTON (*J Biol Chem* 1926 v 69 625) and it was found that the agreement between the two methods was practically as close as between duplicates by either method The serum protein determination was checked by the Kjeldahl method in 12 out of 14 cases there was agreement within  $\pm 0.5$  gm. per 100 cc. the other two showing differences of +0.7 and -0.8 gm. respectively

In normal and most pathological blood an approximate calculation of the haemoglobin can be made from the whole blood specific gravity alone if the mean normal value of the specific gravity of plasma is assumed to be 1.0264 In 47 of 50 cases the results were within 1.5 gm. of the figures obtained from the specific gravities of both whole blood and plasma and except in gross hyperproteinaemia the specific gravity of whole blood alone may be used to determine the haemoglobin and is reliable within  $\pm 2$  gm. per 100 cc.

The haematocrit values obtained from the specific gravity were compared with the direct determinations by the centrifuge the standard deviation between the two sets of haematocrit values in the authors' patients was  $\pm 2.6$  cc. of cells per 100 cc. of blood whereas that for the normal blood specimens of Phillips *et al* was only  $\pm 1.2$  ASHVORTH and ADAMS [this *Bulletin* 1942 v 39 164] found the mean deviation of gravity-calculated haematocrits from centrifuge haematocrits to be three times as great in series of pathological blood as in series of normal blood specimens in 51 of 53 cases the present authors found the gravity-calculated haematocrit values to be within  $\pm 4.4$  cc. per 100 of the centrifuge values the other two cases showed deviations of +9 and -8 cc. respectively A preliminary comparison of gravity and centrifuge haematocrit values would exclude thus 4 per cent. of large deviations and then the gravity method could be used afterwards during the clinical course of the disease.

It was found that red cell counts could not be estimated sufficiently accurately from the haemoglobin in cases of anaemia for normal blood the equation is millions R.B.C per cu mm. = Hb (gm. per cent.)  $\times 0.325$  If the colour index is normal the rapid gravity method may be used to estimate changes in the cell counts during treatment

The other equations are as follows —

- |   |                          |
|---|--------------------------|
| 1 Gm. protein per 100 cc. plasma                  | $= 389.6 (G_P - 1.0079)$ |
| 2 Gm. Hb per 100 cc. blood                        | $= 33.9 G_B - G_P$       |
|   | <hr/>                    |
| 3 Gm. Hb (approx.) per 100 cc. blood              | $= 480 (G_B - 1.0264)$   |
| 4 Haematocrit (cc. cells per 100 cc. blood) = 100 | $(G_B - G_P)$            |
|   | <hr/>                    |
|   | $1.0970 - G_P$           |

$G_B$   $G_P$  = specific gravity of blood and plasma respectively

J F Corson

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

KARR, S. L. & KARR, E. *The Practice of Social Medicine. Clin Proc* Cape Town. 1945 July v 4 No. 5 284-307

The principle of the Health Unit in countries in which the standards of the people are low or in which rural hygiene is rudimentary are not new but have not yet been as widely applied as they could be. The Unit with which the authors are connected was instituted at Polela, Southern Natal, in 1940 (see this *Bulletin* 1944 v 41 611) and has now extended its activities so that 720 homes comprising about 5000 people are constantly visited by and have become well known to the staff.

The objects to which those who undertook this venture set themselves were not confined to the treatment and prevention of disease as those matters are generally understood by clinicians and public health workers. The element of social medicine, which involves close study of the homes economic position, mentalty beliefs and characters of the members of the community was an essential part of the programme of work. It was not enough to know of the existence of disease and to cure it or to prevent it by public health action: the disease was rather regarded as one manifestation of a group of events or conditions, and it was held that elimination of that kind of disease in the future would not be possible so long as the basic conditions which gave rise to it or in which it could flourish, continued to exist. In such public health matters as water supplies and refuse disposal, of course this line of thought is not new: what is new in the work of this unit is the fact that attention is paid to many factors beyond those normally considered to pertain to sanitation. In this way curative medicine and public health activities were combined in one unit which practised social medicine in its full implications: only thus can that human understanding of the people be achieved which is necessary if medicine is to fulfil its purpose.

The Unit consists of a medical officer in charge, an assistant medical officer "medical aids" nurses health assistants and general labourers. It acts in close co-operation with the education and agricultural services in the area, and it conducts clinics school medical work and routine visits to the homes of the people. In this way and by constant consultation and pooling of information, the home backgrounds become well known and the characters habits, economic standards, movements and inter-relationships of the people are studied. Instances of the bearing of these factors on the health of adults and children are given in the form of detailed descriptions of homes and persons belonging to three families. The people are often illiterate and are strongly attached to belief in witchcraft. They are often lazy and make little attempt to improve their condition: they misuse their land, with the result that soil erosion occurs and crops are poor: malnutrition is therefore common. The men are often compelled to leave their homes for long periods, to earn money in the towns but some of them do not use the money to support their families. Alcoholism is common. In such circumstances there is considerable apathy and resistance to change of habits. In its educational and medical activities the Health Unit is gradually breaking down this poor and static mentality but the difficulties are very great.

To the reviewer it seems that the work of this Unit is admirably conceived. It must in time show to the people that the staff of the Unit has an interest in the welfare of each person as an individual, and it will gradually prove to them that the superstitions to which they are now so firmly attached have no basis in fact. This process will, no doubt, be slow but there is no valid reason why Africans should be more unable than others to rid themselves of such ideas.

The transition from an old tribal organization with its clearly understood loyalties and objects to a more modern and critical community must be painful and disappointing in that the removal of beliefs leads to cynicism unless they are replaced by progressive ideas equally strongly held. One of the most important of these ideas must be that the individual is valuable to the community and that the community welcomes whatever contribution the individual can make and is concerned to maintain the dignity of the individual. Here medicine impinges on the field of political psychology and organization as much as on that of economics. Medicine must more and more strongly insist that the health of the people depends to an enormous extent upon their mentality and economic status—that these in turn depend upon the level of general (and not only medical) education and political status improvement in which entails active co-operation between government and people for the benefit of both—and that if any one section of a population regards the protection of its health as a human right there can be no valid reason why that right is not common to all sections. There are indications that the South African Government appreciates the force of such arguments and that it is prepared to act upon them by the inauguration of schemes in which the state of mind of the African is given its proper importance and by which his economic status will be improved so that he will take a personal interest and pride in his own progress and welfare.]

Charles Wilcocks

PINTO C. Um ano de combate às doenças parasitárias que atacam os rodoviários da estrada Rio-Bahia 1942 a 1943 [Parasitic Diseases in the Labourers on the Rio-Bahia Road. One Year's Experiences during 1942-43.] *Mem. Inst. Oswaldo Cruz* 1944 June v 40 No 3 209-340 39 figs & 12 pls (11 folding). English summary.

The service created to cater for the people engaged in this road work was of considerable scope and comprised a central laboratory and an emergency hospital with transport for the sick. The organization is described in detail for which the original should be consulted.

The chief diseases encountered in these labourers were malaria, schistosomiasis, yaws, amoebiasis, hookworm infestation, scabies and the common infectious diseases. The commonest malaria parasite was *Plasmodium vivax* but *P. falciparum* was also often found and *P. malariae* infections are now reported for the first time from the State of Minas Geraes. Experiments on the control of spread of *Schistosoma mansoni* were made by the use of extracts of the stems or fruit of certain saponin-containing plants (*Serjania*, *Sapindus saponaria*) which contain 14 and 12.4 per cent of saponin respectively. These extracts are fatal to snails (*Australorbis glabratus*) and cercariae within a few minutes. An experiment to infect the hairy armadillo *Euphractus sexcinctus* with *S. mansoni* was successful. This animal was found to be naturally infected with *Ancylostoma caninum*.

Charles Wilcocks

GONZÁLEZ R. D. Algunos datos sobre la patología de la región de Tingo María. [Notes on Disease in the Tingo María District, Peru.] *Rev. Méd. Peruana* 1945 Feb v 18 No 194 33-68 4 figs [16 refs.]

Helminthic infestation is very rife according to the hospital laboratory records the incidence is 100 per cent. The commonest worms are *Ancylostoma duodenale*, *Trichuris trichiura* and *Ascaris lumbricoides*; one-third of the children are sent to the hospital by their mothers with a history of having vomited *Ascaris*. It is frequent to see 8-10 ova of hookworm and *Trichuris* in every field of the microscope. Intense hypochromic anaemia is common with

group follows with too little discrimination the results established in temperate regions. Nicholls adopts a position mid-way between the two and if the reviewer disagrees from certain of the conclusions of the book he wishes to make it clear that Nicholls has behind him a large weight of medical opinion in the tropics.

At present the field of nutrition in temperate regions is dominated by what might be called the optimal school of thought. To explain what is meant by this vitamin C may be taken as an example. It is common knowledge that the clinical disease, called scurvy is produced only when for many months a person has taken very low amounts of ascorbic acid. After the recognition of this fact the tests for sub-clinical scurvy were refined and it has been recognized that, although there may be no scorbutic haemorrhages the intake of ascorbic acid may be inadequate to ensure the speedy healing of wounds, and that other morbid conditions may arise. It is unfortunately true that it is quite impossible to say where this state of sub-clinical scurvy fades into normal healthy nutrition, and laboratory tests for saturation with vitamin C are probably artificial and yield fallacious results. Nevertheless, in view of all the known facts, nutritionists in temperate regions have agreed to advise an intake of ascorbic acid sufficiently high to guard against any reasonable fear of a deficiency. With our present spectacles we cannot detect the first signs of wear and tear that is the case for the optimal school of thought. The position of the present reviewer is that we should only lower these standards, fairly reasonably established in temperate regions to suit the inhabitants of the tropics when original observations confirmed by several workers, suggest that there are certain racial or climatic variations peculiar to the warmer regions of the earth. It may well emerge that certain food constituents are needed in increased amounts in the tropics, sodium chloride is a case in point others may be needed in decreased amounts, as calories to supply heat loss but these estimates must be based on original work conducted in the tropics. If there is not enough food in the tropics to give its inhabitants the diet they require and there is certainly not enough at the present time we may bow to necessity but we will never lower our conception of the truth.

Of all the food constituents required by man there is more certain knowledge concerning calorie requirements than anything else. Indeed in the question of calories we need not take the approach of the optimal school of thought too few calories will mean either loss of weight or inability to do hard work too many calories adequately absorbed will mean an increase of weight. Hunger and a sense of repletion maintain most of us in a delicately adjusted state of weight equilibrium. Let us see how the author approaches this problem.

The discussion of calorie requirements commences on pages 164-172, where it is broken up into two or three portions with paragraphs about protein and fat requirements in the middle. Under basal metabolism on page 165 there is no clear statement that B.M.R. depends on surface area none of the recognized formulae, such as that of Du Bois is given, so that B.M.R. cannot be calculated from a knowledge of the surface area which any given weight and height will produce. Nicholls states that a reduction of 10 per cent in the B.M.R. can be allowed for the inhabitants in the tropics, and indeed some reduction is fairly generally accepted, but no reference is made to original observations on this crucial point. There is no clear reference to the Specific Dynamic Action (S.D.A.) of foodstuffs usually taken as about 200 calories in temperate regions which must be added to B.M.R. before the base-line to maintain body weight at rest can be drawn. On page 166 Lusk's estimate of the B.M.R. (no reference attached) is given as 1,680 calories for a 70 kgm. man in temperate regions. Incidentally if the height of this 70 kgm. man is 5 foot 11 inches then according to the Du Bois formula, B.M.R. (not including S.D.A.) would be about 1,800 calories. The former figure of 1,680 calories is

regarded by the author as too high and is reduced to 1 500 as most of the smaller races of the tropics are not 70 kgm in weight. Then follow the suggestions of the League of Nations Report (1936) advocating 2 400 calories for a man or woman living an ordinary life in a temperate climate but not engaged in manual work. This figure of 2 400 calories is reduced by the author to 2 100 calories (page 172) that is a reduction of 300 calories although the suggested reduction in B.M.R. for the inhabitants of the tropics (page 166) was only 180 calories. To this figure of 2 100 calories to cover ordinary everyday living the author adds 400-500 calories for the work of an average labourer in the tropics. No comment was offered on the League of Nations Report (1936) given on page 166 concerning the calorie requirements for work so that unless the mechanical efficiency of the labourer in the tropics is better than that found in temperate regions (usually in the region of 20 per cent like that of a petrol engine) then these 400-500 calories for work are adequate for 6 hours of light work, or 4 hours of moderate work, or 2 hours of hard work, or 1½ hours of very hard work. Some of us would like to add that in our experience the labourer too often in the tropics only does this amount of work and we have suspected that one of the main reasons is that he does not get enough to eat.

Protein requirements are far more generously dealt with in this book. An allowance of 65 gm is quoted on page 173 on the advice of a single authority and appears to be the final conclusion of the author. This conclusion is given as a small sub-section of a discussion on the calorie requirements. Previously the author gives without comment on page 166 the League of Nations (1936) recommendation of 1 gm. of protein for 1 kgm. of body weight in the adult. If the average weight of the labourer of Southern Asia is 52 kgm (page 172) then in the opinion of the reviewer 52 gm. of protein would appear adequate. As a matter of fact most of the discussion on protein requirements is given in chapter I pages 9-23 and it is difficult to understand from this section whether the author feels that the figure of 18.75 gm. of protein (page 14) is grossly inadequate or needs considerable addition. No final opinion is given in chapter I but one is referred at its end to dietary protein allowances in chapter IX. On referring to this chapter on page 156 one finds it misprinted chapter XI but in any case it refers only to condiments and beverages. The reference at the end of chapter I probably refers to chapter XI pages 167 and 173 but in any case one feels that the question of protein requirements has not been handled as a coherent whole.

The reviewer does not wish to stress the viewpoint of the optimal school any further especially in the less certain field of mineral and vitamin requirements. These are dealt with and their uses discussed in chapters II-VIII. The discussion is good and the facts are carefully recorded. Mention is made of the increased needs for common salt in the tropics. In subsequent editions it will be possible to discuss the deficiency that arises in heat-exhaustion. The parts concerning calcium are good. The author is of the opinion that an adult in the tropics may require 0.5-0.7 gm. and a child 0.5 gm. The latter is about half the amount usually suggested in temperate regions.

The anaemias found in the tropics are described on page 40 under iron requirements. Their classification on this page according to the colour index and cell diameter is based on a false premise namely that the colour index should always be exactly 1.0 and the corpuscular diameter should be exactly 7.2  $\mu$ . Iron-deficiency anaemia and the liver principle-deficiency anaemias are classified, and as Nicholls suggests these anaemias are frequently combined. The reviewer has suggested that this combination might be called dimorphic anaemia. The name however is not important, provided the combination is recognized but the author ascribes the term diphasic anaemia to the reviewer (page 45).

The vitamins are adequately and accurately described. Excellent tables on the analysis of foodstuffs are appended. The sections which deal with public health measures are some of the best in the book but more might be added on the dependence of improved nutrition on agriculture the prevention of soil erosion, the question of rents and methods of land tenure. In urban economy the question of a minimal scale of wages, and of feeding labourers as well as canteens at factories might all be added.

One hesitates to make suggestions concerning additions to a book but in future editions it might be wise to add sections on fluid intake (a neglected subject among nutritionists) and infant feeding on the breast or by the bottle. As a clinician the reviewer would welcome a clinical section in which first of all the classical diseases, such as beri-beri and pellagra are described. The modern tendency in books on nutrition is to append pellagra to the section on nicotinic acid but this strains the truth for pellagra is probably always a multiple deficiency disease. After this section on the recognized deficiency states there might follow notes on the less clearly defined conditions, the aetiology of which is unknown or uncertain, e.g. cirrhotic plasma protein anabior malities, crani pavement dermatosis, deficiency, bowel pattern. These are given, with considerable justification, as indefinite types of malnutrition on page 153. As one of these indefinite types there is given Barlow's disease but infantile scurvy is generally recognized and has a precise picture aetiology and treatment. The other indefinite types of malnutrition include "mandama, kwashiorkor, culebrilla, Giffan's oedema, pellagroid-beriberi. Those who have been interested in the kwashiorkor (misapelt kwashiorkor) syndrome of malignant malnutrition in Africa and the West Indies feel that it is probably premature to accord recognition to this syndrome in any textbook. We would like to see the very weighty reasons against its recognition presented fairly thus mandama (pages 234 and 236) is the name employed in Ceylon for what may be rickets. All the other terms on page 153 refer to the same clinical syndrome, described originally and accurately by Cecil (misapelt Cecil page 153) Williams on the Gold Coast as kwashiorkor. Future work on this syndrome may reveal that it is a mixture of deficiency states, or that it is semi-starvation or general malnutrition. Briefly speaking the difficulties in tropical Africa are very great the diets are grossly inadequate by any standard, including that advocated in this book yet little recognized malnutrition is present though much kwashiorkor exists. Whether it is present, perhaps considerably modified, in Asia must remain as yet an open question. Meanwhile oedema, crani pavement dermatosis diarrhoea (page 152) soapy stools (page 154) and fatty livers (page 154) appear to be common. These are all features of the kwashiorkor syndrome.

H. C. Truend.

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## HETEROGENEITY OF STRAINS OF POLYMORPHIC TRYPANOSOMES ITS RELATION TO NATURAL AND EXPERIMENTAL TRANSMISSION

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It is probable that every case or nearly every case of sleeping sickness is curable by Germanin in the early stage largely owing to the discovery of this drug better control of the disease is now possible than formerly. Sleeping sickness is still, however one of the most important and fatal diseases in tropical Africa as many infected persons are already in an advanced incurable stage when first treated.

Several important and interesting questions require further investigation the disease varies greatly in clinical severity in different areas being very acute where the Rhodesian form prevails and comparatively mild, in its early stage in Gambian sleeping sickness areas. These differences as is shown by the character of the infections in inoculated laboratory animals, are due to differences in the trypanosomes, some being more virulent than others. Differences in clinical severity are also found in a single area and may be attributed chiefly to differences between strains of trypanosomes as well as to differences in individual resistance in the population.

The incidence and significance of inapparent mild or chronic infections in areas where the disease is mainly acute seem worthy of investigation. The old problem of the relationship of the three so-called species of polymorphic trypanosomes to one another including the question of reservoirs of human trypanosomes in domestic and wild animals is an important one which needs further inquiry. A closer examination and analysis of strains of polymorphic trypanosomes than has hitherto been made is required.

### *Species of Polymorphic Trypanosomes*

The three species of polymorphic trypanosomes are considered by most observers to be indistinguishable from one another morphologically but they show broad somewhat ill-defined physiological differences. *Trypanosoma rhodesiense* is only distinguished from *T. brucei* by being known to have infected man the two human trypanosomes *T. gambiense* and *T. rhodesiense* differ in degree rather than in kind in respect of certain qualities—the severity of the infection in man and animals sensitivity to arsenical and antimonial



compounds, the numbers of posterior-nuclear forms in animals their geographical distribution, and their principal insect vectors in nature. Both types of human trypanosomes are known to occur in the same territory though one or the other usually predominates, and strains with intermediate characters have been reported (LESTER, 1933). Whether they should be regarded as forming one species or two is still unsettled but however they may have originated, it is convenient to speak of them by separate names. It appears to be probable that mixed infections occur—*T. gambiense* and *T. rhodesiense* in man and either of these with *T. brucei* in animals—as there has been ample opportunity during the last thirty years for their introduction into each other's territories. No investigations of this seem to have been made.

### Strains.

Laboratory strains of polymorphic trypanosomes are the descendants of samples taken from the blood (usually) of naturally infected persons or animals and their previous history is of course unknown but every strain when isolated, and at least for a considerable time afterwards must be regarded as being of heterogeneous composition. Although after repeated mechanical transmissions in small laboratory animals an originally polymorphic strain becomes less polymorphic, perhaps through selection with or without adaptive change the trypanosomes still show physiological differences and like all populations of living things except perhaps clones (descendants of single cells) the strain remains to some extent heterogeneous in composition.

All the trypanosomes of a human strain were of course able to infect or at least to live in the individual from whom the strain was taken—they were not at that time all necessarily able to infect other persons: and possibly none of them could infect certain very resistant individuals—in fact if such a strain of *T. rhodesiense* had been isolated from a naturally infected animal, for example a sheep or an antelope (infected from man by tsetse) and had been tested only on such very resistant persons, it would probably have been called *T. brucei*.

### Selection

The question of what changes may be brought about in collections of living organisms by random sampling and special selection (apart from alterations in protoplasm) is an old subject. That selection must occur during the transmission of polymorphic trypanosomes from one host to another has naturally long been recognized—it is critically discussed by ROBERTSON (1929) in her paper (*vide supra*) on *Bodo caudatus*. When the sequence of events in cyclical transmission is considered, the importance of selection seems obvious, but it has not been definitely proved and should be investigated.

In the first vertebrate host the composition of the strain must be constantly changing—the numbers of trypanosomes in the peripheral blood are known to fluctuate at short intervals and the morphological picture (whatever significance this may have) also changes in respect of the relative proportions of the long and slender intermediate and short and stumpy forms of a polymorphic strain—relapse strains with different immunological characters are formed. Hence a single tsetse fly feeding on the same infected animal or man on different occasions would take up different samples of trypanosomes, and two or more flies feeding at the same time would not necessarily take up samples identical in composition.

In the tsetse fly also it is at least very probable that further selective changes in the strain would occur—in the same fly at different feeds, and in different flies, different numbers of trypanosomes, from none to many would survive

in the gut. Great differences are observed in the proportions of flies infected in experiments with the same strain of trypanosome and the same species of animal and tsetse. There are no doubt several causes of this but little is known about them. Similarly it is reasonable to think that the composition of a population of trypanosomes in the salivary glands of the tsetse fly must vary from time to time in the same fly and in different flies in a single experiment. By a modification of the method used by BRUCE and his colleagues (1913) BURTT (1943) has shown that a tsetse fly ejects in the act of biting different numbers of trypanosomes on different occasions. These quantitative differences may well imply qualitative differences also such as for example varying proportions of trypanosomes of high and low virulence and on some occasions no doubt none sufficiently virulent to produce infection in a host which on another occasion would be infected by the same fly (recorded in man by FAIRBAIRN 1943).

Finally the second vertebrate host would exert a selective influence on the strain when the fly bit it, some of the trypanosomes being able to infect it and others unable to do so.

From some experiments it was concluded that the infectivity of a strain depends upon the number of trypanosomes injected—by the syringe (KLIGLER & RABINOWITCH 1927) or by a tsetse fly (FAIRBAIRN 1943) yet infection has often been produced by the injection of a single trypanosome and the greater chance of the inclusion of the most infective trypanosomes in the greater number a qualitative difference might well explain the results. CORSON (1934) found no appreciable difference between doses of 200 and 100 000 trypanosomes of a virulent strain. The view that mere numbers affect infectivity may be correct but it has not yet been conclusively proved. The question might be decided by work with clones.

Individual differences among the trypanosomes of a strain are apparent in many laboratory experiments. Trypanocidal drugs and sera for example do not kill all the trypanosomes simultaneously and often some trypanosomes survive as was frequently observed long ago (LEVADITI & MCINTOSH 1910). Some of the trypanosomes of a strain show greater sensitivity than others to light or ultra violet rays after treatment with acridine compounds (v. JANCsó 1931 1932 OESTERLIN 1936 HAWKING 1938) relapse strains may be developed from survivors of the preceding strain.

It is therefore probable that selection plays an important part in the transmission of polymorphic trypanosomes in nature and in experiments.

### *Protoplasmic Changes*

Apart from the effects of selection a strain may possibly undergo variation in course of time by actual protoplasmic changes in the trypanosomes. This has been shown to occur in other protozoa.

WENYON (1926) mentions evidence obtained by JENNINGS and by MIDDLETON proving that after long periods of multiplication definite inheritable variations do occur in the descendants of a single individual and this quite apart from any sexual process. It therefore seems probable that if the observations were continued for a sufficient length of time it would be possible to separate from the descendants of a single individual various races which would be as distinct from one another as the naturally occurring races. If this were not so it would be difficult to understand how evolution could take place at all. The subject is clearly dealt with by JENNINGS (1920) in a published series of lectures.

ROBERTSON concluded from her experiments on the action of acriflavine on cultures of *Bodo caudatus* that changes in the body of the protozoon were

produced, and found also that variation occurred in an untreated clone (the descendants of a single *Bodo*) during two years of culture.

JOLLOS (1921) exposed clones of *Paramecium* to arsenious acid and found that increased resistance to the chemical developed and persisted during growth in a normal culture medium for several months but it was gradually lost when the descendants of an isolated conjugating pair were tested it was found that the arsenic resistance had completely disappeared, indicating that the resistance was not a genetic change. In some cases however by long exposure to arsenic a fall in resistance occurred which since it remained after conjugation, was regarded by Jollos as a genetic change.

The loss by old laboratory strains of polymorphic trypanosomes of their transmissibility by tsetse flies appears to indicate an actual change in the trypanosomes.

### *Persistence of Changes*

OZILIER's (1913) experiments with a strain of *T. brucei* are well known—he made a clone resistant to salvarsan and carried it on by inoculation of single trypanosomes and the subclones were just as resistant as their ancestral clone. He mixed salvarsan-resistant and normal clones of *T. brucei* and inoculated the mixture from mouse to mouse and was able to distinguish the strains by testing with a solution of salvarsan, the normal trypanosomes being immobilized after many passages the resistant strain was crowded out by more rapid multiplication of the normal strain. He re-isolated the two strains from the mixed infection by inoculations with single trypanosomes. In these experiments there appears to be no selective process in the development of arsenic resistance.

Clones of trypanosomes were also used by v. PROWAZEK (1913) and by BROWN & BROWN (1937 1938 1939 1940) in their study of variation in *T. brucei*.

The loss of the kinetoplast which may occur spontaneously or be produced by the action of chemicals—oxazine pyronum and other substances—has been regarded as an inheritable structural change. WERBITZKI (1910) found that within 24 hours after the injection of oxazine into a mouse infected with *T. brucei* 80-90 per cent. of the trypanosomes had no kinetoplast and in the case of pyronum 40-60 per cent. The peculiarity was retained through many mechanical passages in animals. WECK (1914) observed "blepharoplastless" [akinetoplasmic] forms in the blood of a waterbuck which was naturally infected with a polymorphic trypanosome while in the case of *T. evansi* also such strains may appear spontaneously in naturally infected hosts (HOARE & BENNETT 1937 1939). HOARE (1940) concluded that the akinetoplasmic condition can be interpreted as a mutation though it also bears some resemblance to cytoplasmic inheritance.

ERLICH and his pupils (1909 1911) and other workers more recently showed that resistance to arsenic can remain unchanged for years in strains of trypanosomes maintained by mechanical passages in animals while YORKER MURGATROYD and HAWKING (1933) proved that it could remain undiminished after two cyclical passages by tsetse flies. EAGLE and MAGNUSON (1944) reported the apparently spontaneous development of resistance to a group of arsenical compounds by a strain of *T. equiperdum* which had not been exposed to chemicals—they did not think that it was a change produced by selection, but that it resembled more a sudden overgrowth of the parent strain by a variant.

It seems therefore that the possibility of the occurrence of heritable change in trypanosomes cannot be excluded, but in a clone spontaneous changes would no doubt be very slow and probably negligible in short experiments.

*Sexual Reproduction*

It is the general opinion that trypanosomes have neither conjugation nor sexual multiplication by gametes the question is critically discussed by WENION VANDERPLANK (1944) from observations on *T. rhodesiense* and FIENNES (1945) from a study of *T. congolense* concluded that sexual reproduction does take place. If this should be confirmed the subject of variation in trypanosomes would be still more complicated and the possibility of hybridization between the so-called species of polymorphic trypanosomes as was suggested by MAXWELL (1936) for malarial parasites would at least need consideration

*Positive and Negative Results*

In transmission experiments with a strain of trypanosomes in which selection plays a part the retention of a character is a positive result in respect of the individual trypanosomes while the loss of a character by the strain is a negative result which could be explained as a loss by the strain of the trypanosomes possessing the character through random sampling or selection. The positive result shows what can happen e.g. the retention of infectivity to man after passages in animals whereas the negative result would not show that any trypanosomes in the strain had lost their ability to infect man as the trypanosomes infective to the volunteers used might not have been transmitted, having been weeded out by selection if the experiment were repeated a positive result might be obtained. In some experiments negative results have so little significance that they should be ignored.

Some positive results have been obtained in experiments with strains of polymorphic trypanosomes where cyclical transmission has been used. As mentioned above YORKE MURGATROYD and HAWKING found in one experiment that resistance to arsenical compounds was not decreased after two successive passages by tsetse flies. Strains of *T. rhodesiense* (DUKE 1935 CORSON 1937 1939 FAIRBAIRN 1943) and *T. gambiense* (VAN HOOFF HENRARD and PEEL 1943) have retained their infectivity to man after repeated cyclical passages through such animals (goats sheep pigs antelopes) as they would be expected to infect in nature. In these experiments the natural mode of transmission from vertebrate host by tsetse fly to vertebrate host was so closely reproduced that there can be no doubt that it occurs in nature although, so far none of the attempts to infect man with polymorphic trypanosomes obtained from naturally infected animals have succeeded there have been few attempts however in sleeping sickness areas

*Validity of Conclusions*

Conclusions and especially generalizations drawn from the results of experiments in which a strain of trypanosomes has shown changes in its characteristics are open to criticism on the ground of the possible effect of selection. Human strains have been stated to have become less or more virulent less polymorphic less or more transmissible by tsetse flies less or more susceptible to the action of drugs or sera even to have lost temporarily at least their infectivity to man. It was concluded from some experiments for example that there were indications that only a certain limited number of individuals of any tsetse population are able to act as hosts for trypanosomes yet in successive experiments with a certain species of reedbuck, 60 33 47 and 52 per cent. respectively of the tsetse flies which lived long enough to become infective had infected salivary glands. An explanation suggested for such an

exceptional result was that the blood of that species of reedbuck was very suitable for the development of the trypanosomes in tsetse flies—further investigations are desirable.

Only when a considerable number of transmission experiments with considerable numbers of flies and animals have produced uniform results may it be permissible to conclude that the trypanosomes have changed—have become say less virulent—this conclusion would apply to that strain and to the particular experimental conditions such as perhaps, the species of animal hosts—it might then reasonably be thought to have been due to the influence of the vertebrate hosts and if they were such as would be exposed to infection in nature the result might have some practical importance.

#### *Uniformity of Material in Experiments*

To test the validity of conclusions and especially generalizations drawn from transmission experiments with strains, it seems to be necessary to try to reduce the variable factors as much as possible. Variation in the vertebrate host could no doubt be much decreased by choosing an inbred strain of mice such as for example the *dba* (Little dilute brown) strain (see SNELL, 1942) and using sufficient numbers—a large mouse population would need to be kept and carefully inbred. Variation within a species of tsetse might possibly be somewhat diminished by using pupae from one locality as different races are known to occur in different areas (BAX 1944). The use of clones of recently isolated strains of polymorphic trypanosomes would probably greatly reduce variation by eliminating selection. It seems to be the only way of analysing a strain of trypanosomes—much could be learned, perhaps, about the effect of selection in transmission experiments by using normal and drug fast clones separately and in mixtures—arsenic fast trypanosomes (which are also acriflavine fast) could perhaps be followed through direct and cyclical transmission, and the same might apply to kinetoplastic trypanosomes in direct transmission. REICHENOW (1940) suggested that the kinetoplast may be essential for development in the tsetse fly. Such labelled trypanosomes might be recognizable in various ways—by testing with the drug to which they are fast by staining, or by measuring their photosensitivity—and might possibly be distinguishable from the “unlabelled” trypanosomes in mixtures, and the varying proportions at different stages of transmission experiments be observed. It would be interesting for example to work with mixtures of *T. brucei* and *T. rhodesiense* one labelled and the other not also to isolate the most virulent clones of strains of *T. brucei* from say Zululand, testing them on man. How far technical difficulties or the behaviour of the clones might interfere with the success of such experiments would probably be indicated in preliminary tests.

These suggestions are offered partly because the ease with which tsetse pupae can now be brought to places outside tropical Africa enables such experiments to be made under good conditions in well-equipped laboratories.

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## SUMMARY OF RECENT ABSTRACTS.\*

### III. MALARIA.

#### *Epidemiology*

RENKONEN (p. 821) discusses malaria in Finland, where the only vector is *Anopheles maculipennis typicus* and *mosaicus*. Incidence curves show a remarkably consistent peak in May (as in Sweden, North Germany and Holland) and the height of this seems to be affected more by the temperature in April than by that of the preceding September—the explanation favoured is that in a cold April the people remain longer exposed than in a warmer April to the bites of overwintered mosquitoes. The author also thinks that the findings are inconsistent with the view that the spring peak is due to a prolonged incubation period after autumn infection.

PEKEPEKEZ Y PALAU (p. 171) describes the malaria position of the delta of the Ebro (Spain) where there is considerable cultivation of rice. *Plasmodium vivax* is the commonest parasite. The fact that at certain seasons relatively large numbers of labourers migrate into and out of this region, and may therefore disseminate their infections makes this a problem of more than local importance.

BUTCHER (p. 335) has summarized what is known of the distribution of malaria and anophelines in Arabia—this cannot further be abstracted.

BOTRICIGUON (p. 172) notes that in the Elisabethville region of the Belgian Congo the chief vectors are *A. gambiae*, *A. fuscipes* and *A. maculipalpis* (the last is not usually regarded as a vector of any importance and the author does not support his opinion by any detailed facts). The malaria of this region is almost all due to *P. falciparum* the local strains of which are very small. He discusses the seasonal incidence of the disease.

GARNHAM (p. 959) reports outbreaks of malaria in a district in the highlands of Kenya (7,500–8,500 feet) where *A. gambiae* (the only vector) and other species of *Anopheles* breed, the former for short periods about May. The mean shade temperature is never high enough for the development of the parasite in the mosquito but *A. gambiae* spends most of its life in human habitations, where the temperature is 5–10° higher than outside. The temperature in these huts, about 66°F., is just high enough for the sporogony of *P. falciparum* in May.

BEET (p. 856) states that *P. ovale* infection is quite common in part of N. Rhodesia. JACKSON (p. 244) reports a case of *P. ovale* infection, presumably contracted in New Guinea where this parasite has not previously been seen.

JACOB and SWAROOP (p. 620) describe the results they have obtained by applying Gill's method of forecasting epidemics of malaria in the plains of

\*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945 v. 42. References to the abstracts are given under the names of the authors quoted, and the page on which the abstracts are printed.

the Punjab considerable precision is attained. In comment WHITE maintains that these predictions have had little value otherwise they would have been falsified more often by appropriate action.

RUSTOMJEE (p 684) describes the epidemiology of malaria in Ceylon, where it is common in the dry zone (*P. malariae* being pre-eminent) moderate in the intermediate zone (*P. falciparum* and *P. vivax*) and rare in the wet zone except for the epidemics which occur from time to time. These epidemics follow deficient rainfall which leads to drying of the rivers with the formation of pools in which *A. culicifacies* the only vector can breed. *P. malariae* plays no part in the epidemics. D ABRERA (p 959) has found that in Ceylon where during epidemics *P. falciparum* displaces *P. malariae* as the most common parasite valuable warning of an approaching outbreak may be obtained by charting the ratio between the two in the blood films examined.

PONS (p 335) has described the physical features of Indo-China in relation to malaria. The chief determining factor is the presence of *A. minimus* which breeds in the valleys of the mountain areas of the country. He claims that certain races of the inhabitants have adapted themselves to life in the unhealthy valleys and have developed considerable resistance to malaria other races have failed to do this.

Although the mortality rate for malaria in the United States was lower in 1943 than ever before FAUST *et al* (p 620) estimate from extensive blood film surveys that there are probably 400 000 infected persons mostly in the Southern States. They call attention to the possibility of spread as a result of malaria (especially *P. vivax*) in returned soldiers. WATSON and RICE (p 173) give an account of malaria as it has been observed in North Alabama during a period of 20 years. *P. vivax* is the common parasite but *P. falciparum* is not rare the mosquito concerned is *A. quadrimaculatus*.

### Aetiology

WOLFERS (p 85) has studied the structure and followed the course of development of *Plasmodium vivax* by means of the electron microscope. Details should be sought in the original.

It is often assumed that the paroxysms of *P. vivax* malaria have a periodicity of exactly 48 hours but YOUNG (p 686) shows that this is not true for some strains in two strains the periods were 43.4 and 45.7 hours respectively. The peak of fever coincides closely with the peak of young ring forms in the blood.

SERGIEV and TIBURSKAYA (p 622) have compared two strains of *P. vivax* one from northern and one from southern Russia by infecting two series of paretic subjects. The southern strain showed much lower parasite counts than the northern strain but more gametocytes and greater ability to infect mosquitoes (probably related to the gametocyte count). There was also some difference in resistance to quinine but not to mepracrine.

BENNISON and COATNEY (p 623) have been able to render sporozoites of *P. gallinaceum* and human blood containing *P. malariae* non-infective by exposure to X-rays.

RUGE and KREMER (p 85) observed abnormalities in malaria parasites which appeared in the blood in spite of suppressive mepracrine. These are described but the details cannot further be abstracted.

### Transmission

GRUNDY (p 517) has compiled and brought up to date a list of *Anopheles* concerned with transmission of disease in man. References are given to the



authorities for the less well known species and in all, 99 species are included, almost all of which are implicated in malaria transmission. The other diseases concerned are filariasis and equine encephalitis.

EYLES (p. 435) sums up present knowledge on the range of flight and dispersion habits of mosquitoes. He gives a table of the maximum flight, so far observed, of 20 important vectors of malaria. In comment MACDONALD makes the point that work on this subject should be extended, since it has so practical a bearing on malaria control. [See also SHAPIRO *et al.* RUSSELL *et al.*, and HUFFAKER & BACK, below.]

GALVÃO *et al.* (p. 4) discuss the rearing and maintenance of mosquitoes in the laboratory in a paper which should be consulted in the original.

RAEVSKY (p. 858) after criticizing the methods used for estimating the numerical fluctuations of a mosquito population, describes his own method, which entails a census of all buildings capable of sheltering mosquitoes and periodical mass collections, or collections in representative sections of the community. He elaborates the uses to which these data can be put.

GERGY (p. 684) has shown that larvae of *A. claviger* (*bifurcatus*) may survive winter in Switzerland, in frozen ponds and slow streams. He has demonstrated that repeated feeding on a gametocyte carrier results in higher infection rates in mosquitoes than a single feed.

A careful investigation of the anophelines of the Dead Sea area of Palestine by SHAPIRO *et al.* (p. 247) has shown that *A. maculipennis* breeds in brackish water puddles (2.5 per cent NaCl) near the shore, in spite of the nightly rise and daily fall of the water level which causes the disappearance of these puddles during the day. The larvae were found 10-15 cm. below the gravel surface in the daytime. *A. sergenti* breeds in swamps fed by springs and though breeding is most prolific from spring to autumn, it continues throughout the winter. Strong evidence was found that *A. sergenti* travels from 4½ to 8 kilometres even the males disperse for long distances so that their presence does not necessarily indicate the proximity of breeding places. *A. superpictus* and *A. maculipennis* breed in the same swamps but *A. sergenti* is the predominant species.

SHUTE (p. 857) has made counts of the number of sporozoites of *P. falciparum* in the salivary glands of infected *A. maculipennis atroparvus*. The numbers vary greatly up to 219 450. If the mosquitoes are allowed to feed on a rabbit every two or three days after the estimated time of first infection of the glands, the numbers of sporozoites in the glands are fairly well maintained for 25 days, after which they decline but there is no uniformity in the discharge of zootoxes.

Little is known of the mosquitoes and of the incidence of malaria in Iran. BEKLEMISHEV and GONTAREVA (p. 248) studied the subject in 1941 in the north-western part of the country. In the uplands *A. superpictus*, *A. maculipennis maculipennis*, *A. sacharovi* and *A. claviger* (*bifurcatus*) are found especially in well-watered country in which standing collections are allowed to form. In the Caspian coastal area, where the climate is sub-tropical, drainage ditches and rice fields are numerous, and *A. maculipennis* and *A. hyrcanus* are found, but in the rivers, where the fish *Gambusia* is present, larvae are not found. GUTSEVICH (p. 533) names the anophelines found in northern Iran. *A. sacharovi* and *A. superpictus* are important in relation to malaria, but *A. hyrcanus* is also found.

BIELOGLAZOV (p. 249) reports the wide distribution of *A. maculipennis messeasi* throughout the Mongolian People's Republic.

An account of the biology of *A. algeriensis* is contributed by ENIKOLOPOV (p. 859). It is not an effective carrier of malaria, though it feeds on man, its mean duration of life being much less than that of *A. maculipennis* usually too short for the complete cycle of development of the parasite.

SAUTET and MARNEFFE (p 336) describe the outdoor resting places of certain anophelines of Lebanon and of the Niger country

MATTINGLY (p 434) has produced new keys to the anophelines of West Africa.

RIBBANDS (p 3) has studied the mosquito which was formerly regarded as the *melas* variety of *Anopheles gambiae* and concludes that the evidence justifies its classification as a separate species *A melas*. This mosquito will breed in water of high saline content. CHWATT (p 860) has studied the morphology and habits of *A melas* in relation to *A gambiae*. The morphological differences in the various stages are not in his opinion sufficiently clear-cut to permit the classification of *A melas* as more than a biological race of *A gambiae* from which it differs mainly in its ecological preferences and geographical distribution. RIBBANDS (p 245) has studied the effect of rainfall tides and periodic fluctuations on a population of *A melas* in Sierra Leone. This mosquito breeds in brackish grassy areas flooded only at high tide and mostly dry in the dry season and in brackish *Avicennia* mangrove areas. The average size of the adult population is closely determined by rainfall and peaks occur 20-30 days after the causative rainfall. Increase is also correlated with high tides in the dry season. *A melas* is present throughout the year but the population in the wet season is ten times as high as it is in the dry season and the influence of tides is not so great as that of rain.

LEWIS (p 246) has studied *A gambiae* around Wadi Halfa with a view to its control first as a protection to the town itself and second for the purpose of creating a barrier which the mosquito (whose breeding is confined to the vicinity of the Nile) cannot pass, so that if it can be eliminated from Egypt north of Wadi Halfa there would be little risk of its infiltration again from the south. *A gambiae* breeds in pools among the islands of the cataract on sandy banks in the river and near its margin these dry up and breeding in them ceases from December to April but the mosquito reappears in April probably because it has continuously been breeding in the cataract area. Control by oiling Paris green and drainage has proved successful and the larvorous fish *Gambusia holbrooki* has its uses.

Working in Brazil in 1939 DE OLIVEIRA CASTRO (p 960) found by experiment that the eggs of *A gambiae* do not survive long if kept away from water even in a moist atmosphere. Survival is rather longer at 14°C than at higher (room) temperature but even then only 0.1 per cent. of the eggs produced living larvae when they had been kept for 20 days at 14°C away from water.

By means of the precipitin test MARNEFFE *et al* (p 247) have found human blood in 55 per cent of female *A gambiae* tested in the Middle Niger region.

WANSON and BERTEAUX (p 337) have found salivary gland infection in *A brunipes* near Léopoldville. It is not a common mosquito and is therefore not an important carrier.

COVELL (p 623) has contributed a comprehensive paper on the distribution breeding places adult habits and relation to malaria of the anophelines of India and the Far East. Of the many species which have been described 41 are concerned with malaria in these areas and the paper deals only with these. They are classified as—12 important vectors, 16 of local importance and 13 having probably no practical importance. During the war the two groups which have been outstanding in relation to malaria are the *fluviatilis minimus* group in India, Burma and S China and the *punctulatus* group (with *moluccensis*) in New Guinea and the S W Pacific.

PURI (p 85) has issued a revised edition of his synoptic tables for the identification of full-grown larvae of the Indian anophelines.

D ABRERA (p 337) describes the eggs of a number of anophelines of Ceylon the original should be consulted for details.

SIDDONS (p. 624) in India has succeeded in infecting 9.4 per cent. of *A. culicifacies* with *P. malariae* and in transmitting the infection by bite to a healthy subject. He found a much higher infection rate in those mosquitoes which were fed in the period August to February than in those fed in March to July when the weather is hot. In those fed in the colder weather the gland infection rate was 34.4 per cent. The extrinsic incubation period varied from 22 days at 70°F to 14 days at 80°F. In the man who was infected by the bite of some of these mosquitoes parasites were first seen in the blood 30 days after the infecting bite, and the first attack of fever occurred 36 days after infection. Following the account of this work is a paper by the same author (p. 625) in which he shows that the optimum temperature for development and transmission of malaria parasites in *A. culicifacies* is 70°-86°F provided that humidity is fairly high. Development of *P. falciparum* and *P. vivax* does not take place above 94°F. The extrinsic incubation period for *P. vivax* is 7 days at 86°F.

RUSSELL *et al.* (p. 637) have performed a large experiment on the flight range of *A. culicifacies* in India. The greatest observed distance was between 1.5 and 1.75 miles in some cases against the wind. The authors have treated their results statistically and for details the original should be consulted.

JASWANT SINGH and JACOB (p. 618) have investigated malaria on the southern coast of the Bombay Presidency. Here the disease is not common on the coastal belt but is hyperendemic in the foothills and the interior. The distribution coincides with that of *A. flavirostris*, the only vector of which, in one place, 11 per cent. were found to be infected. It breeds in slow running streams. *A. culicifacies* and *A. annalis* were also found, but there was no evidence that in this area they act as carriers of malaria. *P. malariae* is the most prevalent parasite.

In part of Hyderabad State where an irrigation project has been in existence for some years, the chief vector is *A. flavirostris* which here breeds in irrigation canals, rainwater pools and seepages. *A. culicifacies* probably plays a small part in transmission. In this area ABRAHAM and SAMUELS (p. 619) found *P. malariae* to be the commonest parasite. A control programme which aims at destruction of adult mosquitoes, larval control, and the use of suppressive quinine has given encouraging results.

VISWANATHAN *et al.* (p. 625) note that most freshly-fed *A. flavirostris* leave their places of feeding before dawn, for some outside resting place. This affects the spray-killing of adults as a method of control, and the authors advocate daily spraying where there is no larval control, or spraying twice a week where larval control exists, or on 2 consecutive days with 2 days rest, in the period September to November when the proportion of the mosquitoes which leave the dwellings at night is highest.

*A. philippinensis* is the only important vector in the deltaic region of Bengal, where the maximum transmission season is from September to November. IYENGAR (p. 625) shows that it favours human dwellings as daytime resting places, and that control should include spray-killing. This species breeds in ponds of clean water and is inhibited by shade. It does not usually breed in rice fields.

KNIGHT and FARNER (p. 638) give reasons for thinking that *Anopheles punctulatus moluccensis* should be known as *A. p. farneri*.

REEVES (p. 437) has carried out precipitation tests on blood from the stomachs of freshly engorged American anophelines of various species.

Hess and HALL (p. 626) note that *A. quadrimaculatus* breeds only in waters on which there is abundance of vegetation or floating material, and have classified the plants which are important in malaria control, from this point of view in the area concerned. SCHOOF *et al.* (p. 628) have shown that larvae

and pupae of *A. quadrimaculatus* and *A. punctipennis* can survive for some days in mud but the precise length of time is not known. BURGESS and YOUNG (p 437) give the results of their investigations into the handling and feeding of *A. quadrimaculatus*. For details the original should be consulted. HUFFAKER and BACK (p 687) have found that *A. quadrimaculatus* does not usually move in significant numbers more than one mile from its breeding place but exceptional circumstances may permit it to do so. A very few individuals may travel 3 miles.

In the Annual Report issued jointly by the Government of Trinidad and the Rockefeller Foundation (p 617) the point is made that *A. aquasalis* is an important vector but that it is strongly zoophilic in habit. It seems that the presence of buffalo stables near a village has a strong effect in keeping down the incidence of malaria in the inhabitants and it is suggested that traps baited with animals may be used in malaria prevention. In the wetter parts of Trinidad transmission is effected by *A. bellator* which breeds in the bromeliads which are parasitic on the shade trees of cocoa plantations. Suggestions are made and experiments have been carried out on the removal or destruction of these plants.

COCHRANE (p 86) has produced circumstantial evidence of some weight that *A. argyritarsis* may be a vector of malaria in Grenada.

BEVIER (p 614) states that *A. darlingi* is the only known vector of malaria in the coastal belt of British Guiana, and that in 1943 it accounted for 96 per cent of all anopheline captures. It almost completely disappeared in the drought years of 1938-41 but reappeared with the heavy rains of 1942-43. It does not seek acid or brackish waters. With the increase in the abundance of this mosquito there was a corresponding increase in the amount of malaria for which *P. falciparum* was largely responsible though *P. vivax* and, to a smaller extent *P. malariae* were found. GIGLIOLI (p 615) also states that *A. darlingi* is the only vector in Georgetown British Guiana where it breeds extensively in the suburbs. It disappeared during the drought but its reappearance after the rains caused an epidemic of malaria. *A. darlingi* breeds in the drainage system of a cemetery and in rice grounds and cane fields; its eggs die in water containing more than 0.6 per cent of NaCl. Where malaria is abundant *P. falciparum* and *P. vivax* are common but during the drought when malaria was rare most of the infections were due to *P. malariae* rarely seen in times of epidemics.

UNTI (p 86) has studied the viability of eggs of certain anophelines of Brazil, when kept in moist earth.

Larvae of certain S. American anophelines die when the dissolved oxygen content of the water is reduced to 1.5 p.p.m. UNTI (p 86) concludes that pollution of water with organic matter by decreasing the oxygen content may be an efficient and economical anti-larval measure. The same author (p 87) has failed to find any correlation between the iron content of water and anopheline breeding.

### Transfusion Malaria

MCCLURE and LAM (p 627) report two cases of transmission of *P. malariae* by the transfusion of blood which had been refrigerated for 5 days. The two donors were Sicilians who had lived for 30 years in the United States, and who presumably had not been infected there.

OFFICER (p 688) has shown by experiment in man that the routine course of anti-malaria treatment given to a recipient immediately after transfusion of malarial blood prevents the disease. In cases of emergency therefore a potentially malarial donor may be used for transfusion.

STOHLMAN (p. 174) reports the transmission of *P. vivax* from an infected patient to three donors of blood transfused directly to him, without storage. There must have been some reflux of blood through the apparatus used. In comment MOLLISON points out that direct transfusion is now very rarely used, but adds that transmission from donor to recipient is possible even when the blood has been stored for some days.

### Tests.

SOBERÓN y PARRA (p. 174) describes an intradermal test for malaria in which the antigen is prepared from the blood of a fowl heavily infected with *P. gallinaceum*. The results indicate a large measure of specificity.

HEIDELBERGER and MAYER (p. 689) have found that an antigen prepared from normal human red blood cells is as effective as (and more readily available than) the antigen prepared from *P. gallinaceum* in the complement-fixation test for malaria. By this test 28 per cent of sera from malarial patients were positive.

BOGEN (p. 861) describes a test which depends on the fact that serum in malaria is precipitated by a stock buffer solution diluted with four times its volume of distilled water. This test is strongly positive during and for some time after an attack. It may be useful in diagnosis or for epidemiological investigations, and in prognosis.

WOOD (p. 250) has found that the red cell sedimentation test provides a useful means of differentiation between malaria (in which the rate is high) and infective hepatitis (in which it is relatively low) in their early stages.

ROSENBERG (p. 440) has investigated six serological tests for syphilis, to determine their relation to malaria. He concludes that, of all the generally accepted tests, the Hinton test gives the smallest percentage of false positive reactions in malaria. That malaria can often be distinguished from syphilis by the pattern of positivity of tests and that persistence of positive reactions beyond 6 weeks, in the absence of continued malarial infection, should arouse suspicion of syphilis. PORTER *et al.* (p. 690) tested 100 men, suffering from malaria (89 *P. vivax*) with the Wassermann and Kahn tests. All had previously given negative results, and were presumably free from syphilis, but 12 were now positive and 10 doubtful. The results all became negative within 30 days (the patients presumably having received anti-malaria treatment).

The sera of a high proportion of patients with malaria were found by COLEMAN (p. 250) to contain the  $V_2$  agglutinins of *Bact. typhosum* in high titre. This may be because the parasite possesses a  $V_2$  antigen or the reaction may be anamnestic.

SHEPHERD (p. 4) has devised a radiological technique for demonstrating the spleen without the use of any contrast medium. Measurement of the size of the spleen can thus be made and the method may be useful in relation to malaria.

### Pathology

RIGDON (p. 689) has found evidence that infarcts of the spleen in *P. falciparum* infection may result from obstruction produced by hyperplasia of cells in the walls of the venous sinuses to which leucocytes and red cells may adhere.

MARSHALL (p. 438) reports a case of spontaneous rupture of a malarial spleen without any history of trauma. Attention is drawn by KIRK and VOORIS (p. 341) to the fact that the liver becomes enlarged, and shows other (biochemical) signs of involvement in half of the patients with malaria. This may occur in a first attack, and is not a sign of chronicity.

DÄHNE (p 338) has found that reticulocytosis occurs in malaria patients who are anaemic about one week after treatment has been started. The blood sedimentation rate is high in such patients but not in patients who are not anaemic.

### Clinical Findings

HUNT (p 5) relates his experience of malaria in West Africa and in North Africa. In the latter subtertian infection was much more alarming and demanded intravenous quinine therapy much more often than in West Africa. He emphasizes the fact which is so often forgotten and relearned at a cost that subtertian malaria is a dangerous disease which mimics other conditions to the confusion of the unwary. It should never be lightly regarded.

FERRIMAN (p 438) writes of his experience in West Africa of 2,000 cases of malaria in white R A F men most of whom had never before been exposed to the disease. Almost all the infections were due to *P. falciparum* but pernicious attacks were not common, suppressive mepacrine (0.2 gm twice a week) being enforced. Positive blood slides were not found in all cases and the author comments on the value of splenomegaly as an aid in diagnosis. Sub-clinical malaria was not uncommon the chief symptom being recurrent headache this was relieved by anti-malaria treatment.

HYMAN (p 962) gives a list of mistaken diagnoses made in 100 men whose illness was subsequently found to be malaria during the early days of the campaign in the Solomon Islands. These were chiefly diagnoses of cardiac pulmonary and abdominal conditions but arthritis diseases of the brain or other parts of the head kidney thyroid and scrotum were also diagnosed. Later an outbreak of dengue added to the difficulty of diagnosis.

GAYID (p 5) notes that in the Middle East *P. vivax* infections were frequently atypical. He gives details of the standard quinine-mepacrine pamaquin treatment adopted in that area.

In the province of Voronezh Russia which at one time in the war was under German domination STEINBERG *et al* (p 339) have found that malaria in children frequently runs an unusual course regardless of the species of parasite which may cause it to be mistaken for other diseases. This may be due to importation of new strains or to alteration in virulence as a result of serial passage through undernourished human hosts. KASSIRSKY (p 628) refers to the fulminating type of *P. vivax* infection which has previously been described in Russia.

BOYD (p 175) has studied the parasite density in persons with naturally induced *P. vivax* malaria, at different stages of the infection. Great variation was observed, for details of which the original abstract should be consulted.

GORDON *et al* (p 692) describe the clinical features of relapsing *P. vivax* malaria in soldiers evacuated from the South Pacific. The strains showed a pronounced tendency to relapse but the attacks were relatively mild and were easily controlled by mepacrine. In rehabilitation the development of physical fitness and the restoration of self-confidence were important.

BOYD and KITCHEN (p 174) give details of their observations on the renewal of clinical activity in naturally induced *P. vivax* malaria both after spontaneous remission and after remission due to administration of drugs. The facts presented are so numerous that further condensation is not possible.

From an experience of the course of malaria in British troops who escaped from Italy into Switzerland, ANDERSON *et al* (p 961) conclude that the influence of a high altitude climate (Adelboden 4,300 feet) is very beneficial in the relapsing benign tertian type.

MCGINN and CARMODY (p 341) describe 16 patients with cerebral malaria, all ascribed to *P. vivax*. FITZ HUGH *et al* (p 340) describe cases of cerebral

malaria among troops stationed in India, noting several cases in which the infection was due to *P. vivax* or *P. malariae* though the majority were due to *P. falciparum*. In a well-nourished group previously in a high state of physical fitness the death rate was much lower than in another group of lower standard though the incidence did not greatly differ. The association of convulsions and coma carried a grave prognosis especially if the parasite count was high on the other hand, in some fatal cases there were few demonstrable parasites. VISWANATHAN (p. 691) discusses the pathogenesis of cerebral malaria, and describes several fatal cases in which a well-formed ante-mortem clot was found in the sagittal sinus. This, he thinks, has not previously been reported.

DAS GUPTA and GANGULI (p. 338) describe a fatal case of *P. falciparum* infection in which large numbers of gametocytes in all stages of development, and of schizonts, were present in the peripheral blood.

In Panama, APPLEBAUM and SHRAGER (p. 176) have investigated 125 cases of pneumonia associated with malaria, chiefly in young white men. The pulmonary lesions were most commonly lobular in distribution. The combination was not severe. In one group the condition yielded to sulphonamide treatment, but in another it yielded to anti-malaria treatment alone. In most of the sputa examined no pathogenic organisms could be found.

ROBERTSON (p. 439) writes on lesions of the eye in relation to malaria. The most common is ulcer of the cornea, often with recurrent iris but optic neuritis and amblyopia have also been found.

MERRILL (p. 691) has observed patients in the United States forces who having had malaria, complain of chills which they attribute to malaria but which are not accompanied by fever and which are of psychogenic origin. ARBUCK (p. 963) makes the point that although neuropsychiatric symptoms may occur in malaria, they are usually consistent with the personality of the patient, and are activated by that disease as they may be by other organic diseases.

HARVEY (p. 963) describes a type of peripheral neuritis associated with *P. vivax* malaria, which was quite common in one large American military hospital.

HARRISON and DAKIN (p. 176) report a case of nephritis, associated with *P. malariae* infection, in the south-west Pacific. It is not certain that the malaria was responsible for the condition, but it is not unlikely.

MANNON BARR and MUGGLETON (p. 434) record a case of unusually long persistence of *P. ovale* infection.

KEAR and SMITH (p. 338) note that if the inhabitants of Panama survive childhood they are unlikely to die of malaria. The number of parasites in the peripheral blood is not a good index of the severity of the case.

Charles Wilcocks

[To be continued]

## RABIES.

### A REVIEW OF RECENT ARTICLES. XLIV\*

#### (i) Virus

BAILEY<sup>1</sup> points out that there is scarcely any "organic liquid, humour secretion excretion or parenchymatous pulp" of which the action on the virus of rabies has not been investigated but, curiously enough, as far as he

For the forty-third of this series see this Bulletin 1945 v. 42, p. 674

<sup>1</sup> BAILEY J. Action de l'extrait de pancréas sur le virus de la rage. *Bull. Acad. Méd.* 1945 v. 129 Nos. 13-14 & 15 253-7

could determine no one had thought of studying the action of pancreatic juice. The author points out (and he has apparently been considering mainly the possibility of proteolytic action) that if he had been able at the time he thought of carrying out his investigations to procure some of Northrop's crystallized preparation of trypsin he would have used that. He decided to use a watery extract of pancreas from a dog and he outlines his method of preparation, which was carried out at low temperature. After the extraction had proceeded for a period of 48 hours he tested the amylolytic effect of the maceration on starch and since such activity was demonstrated he believed he was justified in his surely hazardous assumption that it would possess proteolytic activity. His virus suspension consisted of a 1:50 suspension of the brain of a rabbit inoculated with a fixed strain of virus. This suspension had been filtered through filter paper to remove the larger particles of tissue. The author states that a number of experiments were performed along similar lines and he has recorded the results of some of these as being typical. Two sets of tubes were put up in each experiment one containing the virus suspension and equal parts of the pancreatic extract and the other the virus suspension with equal parts of physiological saline. The alkalinity of the mixtures was adjusted (somewhat crudely) by the addition of sodium carbonate but he does not state clearly what indicator he used. The recorded pH values of the mixtures ranged between 10 and 12 and were stated to be similar in the control tubes. The mixtures were kept at 10°C for 24 hours. The results of two experiments are recorded in one 4 mice were inoculated with the mixture of virus with pancreatic extract and 2 mice were inoculated with the mixture of virus with pancreatic extract and 2 with the virus in saline and in the other 2 guinea-pigs were inoculated with the pancreatic-extract virus mixtures and 2 guinea-pigs with the control mixture without pancreatic extract. The 4 mice and 5 guinea-pigs inoculated with the virus-pancreatic-extract mixtures survived and the 2 mice and 2 guinea-pigs inoculated with virus alone died of rabies. The author concludes that the virulence of brain suspension was destroyed by the aqueous extract of pancreas of a dog in 24 hours at 10°C. He also made some experiments in which he states that the recorded pH values of the several mixtures of virus with or without pancreatic extract ranged between 6 and 8.4 (in one of these experiments a 'street' strain of virus was employed instead of a fixed strain and in the other the strain is not stated). In these tests also only a limited number of animals were inoculated with the mixtures a total of two rabbits and four guinea-pigs with the mixtures of pancreatic extract and virus and one rabbit and two guinea-pigs with the virus mixtures and all the animals died of rabies. The author concludes from a consideration of all the results that since the destructive action of the pancreatic extract on the virus of rabies was dependent on the alkaline reaction of the medium this shows that it was due to the activity of trypsin and that the destructive action on the virus was proteolytic in nature. [Some of the details of these experiments have been stressed because it is felt that it would be unfortunate and misleading if they were subsequently referred to as conclusive evidence of the destructive action of a pancreatic extract (or trypsin) on the virus of rabies. Surely it would be necessary to make such studies on a quantitative basis especially as regards the relative virus content of the original suspensions (a gradocol filtrate would be preferable) and the control mixtures without pancreatic extract at such a high alkalinity as pH 11 or 12. The stability of the virus in media of different pH values should form the subject of a preliminary investigation. It might quite well be that the amount of virus surviving in certain hydrogen ion concentrations is low and if few test animals are inoculated the probability of detecting virus would be a question of chance. The optimum pH value for tryptic activity is less alkaline than pH 11 to 12 and although trypsin would be to a certain extent protected by



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protein in the substrate one would expect the activity of trypsin to be much reduced above pH values of 8-9.]

KANAZAWA (this Bulletin 1937 v 34 671) WEBSTER and CLOW (ibid 1938 v 35 641) and 1941 1938 v 35 168] BERNKOPF and KLIGLER (ibid 1938 v 35 641) reported the successful cultivation of fixed strains of rabies virus in relatively simple media consisting of fragments of rabbit mouse rat or chick embryo brains in Tyrode's solution. Whereas KANAZAWA did not add serum to his medium, WEBSTER and CLOW incorporated 10 per cent monkey serum and BERNKOPF and KLIGLER recorded that they found the addition of human or monkey serum, but not rabbit serum, to be favourable to the multiplication of the virus. Subsequently WEBSTER (this Bulletin 1938 v 35 646) KLIGLER and BERNKOPF (ibid 1939 v 36 723) and HODGES WEBSTER and LAVIN (ibid 1941 v 38 161) reported on the antigenic value and potency of vaccines prepared from such tissue cultures. The virus potency of the tissue cultures or dogs infected intracerebrally with fixed rabies virus. The last-named authors therefore attempted to increase the virus content of the tissue cultures by several methods without success but they obtained a 10-fold concentration of the culture virus by freezing and drying. WEBSTER and CASALS (this Bulletin 1942, v 39 82) stated later that from a practical point of view culture virus had not proved a satisfactory source of rabies vaccine due chiefly to its low virus content.

In later experiments on the vaccination of mice and dogs WEBSTER and CASALS (this Bulletin 1941 v 38 499 and 1943 v 40 201) reverted to fresh brain material from mice and dogs infected intracerebrally with fixed rabies virus as a source of antigen for vaccine production. (It is interesting to note that FLOTZ and REIGAS (this Bulletin 1942 v 39 589) reported the successful cultivation of street strains of virus in culture media consisting of chick-embryo brain tissue in Tyrode's solution with monkey serum and chicken plasma.)

PARKER and HOLLENDER<sup>1</sup> now bring confirmation of the possibility of propagating "fixed" strains of rabies virus in tissue cultures similar to those used by the earlier workers. They have extended the observations of the latter and have recorded a number of interesting findings. They used different strains of "fixed" virus that had been passaged for various periods in mice. The "Squibb" strain had been passaged 12 times in mice the Webster strain 128 times and the Alabama strain 109 times. The Alabama strain gave the best results in that the cultures appeared to have a higher virus potency but as the technique was modified it would be difficult to associate these results with any special attribute of this particular strain. Finely chopped embryo mouse brain was used as the tissue component of the medium (one large brain or its equivalent being used for each culture. In the early experiments the fluid phase of the culture consisted of heated rabbit serum (1 hour at 66°C) (constituting  $\frac{1}{2}$  or  $\frac{1}{3}$  of the final mixture) and of ox serum ultrafiltrate (1) (see SAKS and SAKS, Arch Pathology 1942, v 33 619) together with 1.4 per cent sodium bicarbonate (1) and Tyrode's solution containing four times the usual amount of glucose. The pH of the mixtures was adjusted to 7.2, by means of a gas mixture before the tissue was added, and thereafter the cultures were gassed with a mixture of

<sup>1</sup>PARKER R. C. & HOLLENDER, Argentina. J. Propagation of Rabies Virus in Tissue Cultures. Proc. Soc. Exper. Biol. & Med. 1945 Oct v 60 No 1 84-8. [Refs 12 footnotes.]

oxygen (21 or 80 per cent) carbon dioxide (8 per cent) and nitrogen. In the later experiments the fluid medium consisted either of heated rabbit serum or ox serum ultrafiltrate (4) combined with Simms's 1/7 solution (see SIMMS and SANDERS *loc cit*). As an indicator of pH all cultures contained either 0.001 per cent or 0.005 per cent phenol red. Another feature of the later experiments was that the culture tissues were ground when passages were made. It had been found by comparative inoculation tests in mice for virus potency with ground and unground tissues that grinding is necessary in order to liberate the main bulk of the virus from the tissues. There was little to choose between the two methods of grinding with quartz sand or with Tenbroeck grinders. In all the later experiments 125 cc Erlenmeyer flasks were used, whereas in the earlier experiments Carrel flasks with only 3 or 4 cc. of medium were used.

Comparative tests with cultures containing heated rabbit serum or on the other hand, ox serum ultrafiltrate showed that beyond the sixth passage in which passage the rabbit serum cultures had a higher titre than the ox serum ultrafiltrate cultures it was not possible to detect any appreciable difference between the two sets of cultures. A duplicate series of cultures incubated for nine passages at 35°C and 37°C respectively showed no consistent difference in the amount of virus produced.

Comparative tests showed also that the subjection of the cultures to continuous gassing with the mixtures of O<sub>2</sub>, CO<sub>2</sub> and N<sub>2</sub> had no real advantage provided that the buffering system in the medium is capable of maintaining the pH value at an optimum level [this optimal level is not stated]. The results of other experiments showed that embryo mouse brain culture virus could be maintained in cultures prepared from the brains of 5-day-old mice; the brains of 14-day-old mice were less satisfactory and the brains of 28-day-old mice [48-day-old mice in the summary] were quite unsuitable. [No mention is made of any attempt to propagate virus recovered directly from the brains of infected mice in cultures with 5-day-old brains.] Unsuccessful attempts to propagate the rabies virus in chick embryo brain cultures are recorded. The source of the virus in these experiments was either virus passaged in mice or in mouse embryo brain cultures or mouse virus adapted to chick tissue by several intracerebral passages in chick embryos in eggs. In all experiments two passages of 3 and 4 days respectively were made each week.

In early experiments with the Squibb strain the virus was successfully passaged 57 times during a period of 28½ weeks at the 41st passage mice were infected with a 10<sup>-6</sup> dilution of the culture tissue but by the end of the experiment the limiting infective dilution had fallen to 10<sup>-2</sup>.

Three experiments two of seven passages and one of eight were made with the Webster strain of virus but at the end of the experiments the limiting infective dilution of the cultures was not higher than 10<sup>-4</sup>. In one of the later experiments with the Alabama strain, with which the most satisfactory results were obtained 19 passages were made and in the protocol of the experiment it is stated that at the 19th transfer (passage) the culture virus killed mice at a dilution of 10<sup>-6</sup> whereas in the summary and conclusions the authors report that the virus multiplied to the extent that mice were killed regularly by the culture material in dilutions as high as 10<sup>-6</sup>. It is not clear whether this represented the limiting infective dilution of any culture of the series or whether some culture passages had somewhat lower virus titres. In the early passages in mouse embryo brain cultures of another series with the Alabama strain, limiting infective dilutions (see Table I) of 10<sup>-4</sup> to 10<sup>-6</sup> are recorded. It would be interesting to know also what the virus titres of subsequent culture passages (if any have been made) prove to be. (The virus titres of the cultures in the experiments with the Squibb strain

appeared to be relatively good up to the 41st passage but later deteriorated very much.)

In the experiments with the "Alabama" strain the limiting infective dilution of the original virus in mouse brain was not determined, but all four mice inoculated with a  $10^{-2}$  dilution contracted rabies.

### (ii) Symptomatology and Diagnosis

RIFKIN *et al.*<sup>3</sup> record that rabies had never been known to exist on a certain large island in the Pacific which came to be used during the war as a base with an important harbour and greatly increased shipping. Dogs were introduced from the mainland and at first it was thought that rabies had been brought in also. This suspicion arose when two dogs which had been kept as pets suddenly became excitable and vicious, had epileptic fits and also bit six marmos. Inclusion bodies which were considered at first to be similar to Negri bodies were found in sections of the brains of these dogs, but no animal inoculation tests were made. A course of Pasteur vaccination treatment was therefore given to the marmos. Later a limited number of guinea-pigs, rabbits and mice were inoculated with brain suspensions of dogs showing similar nervous symptoms, but no rabies developed in these test animals. The incidence of dog distemper on the island was very high and the clinical pictures of the nervous cases were identical with those recorded in rabies. A veterinary surgeon who was a member of the team brought four cases of nervous distemper for investigation, and inclusion bodies similar to but not characteristic of Negri bodies of rabies were found in sections of their brains, trachea, bronchi and bladders. Inoculation of guinea-pig, mouse and rabbit with suspensions of brain gave negative results. The inclusion bodies could be found in the ganglion cells of the cerebrum, mid-brain, medulla and in the Purkinje cells of the cerebellum. They were found in sections of the medulla and *Cornu ammonis* of the first two dogs referred to above. They were about 2-10 $\mu$  diameter oval in shape stained red with Mann's stain and in certain cases had a vacuolated structure but without internal granulations as seen in rabies. The authors cite a reference in 1943 to the occurrence of such inclusion bodies in the brain and other organs of dogs infected with distemper and point out that their occurrence might lead to a mistaken diagnosis of rabies if animal inoculation tests are not made also. The inclusion bodies under discussion, which are associated with cases of nervous distemper in dogs, are commonly known as Lentz bodies. They were first described by that author in 1907 (*Cent. f. Bakt., 1. Abt. Orig.* v 44 374). Descriptions of these bodies are found also in papers by BARTS and SIAROVICI, 1912 (*m. C. R. Soc. Biol.* v 73 229), SINIGALLA 1913 (*Pathologica* v 6 107) and KAKTOROWICZ and LEWY 1922 (*m. Arch. wiss. prakt. Tierhik.* v 49 137) and others. GREEN and EVANS 1939 (*m. Cornell Vet.* v 29 35) recorded their occurrence in the tissues of foxes, mink and ferrets infected with distemper.]

RODRIGUEZ<sup>4</sup> has compared results obtained in diagnosing rabies by histopathological methods with those secured by inoculating groups of five mice with suspensions of brain tissue from the suspected cases of rabies. The former methods included examination of smears and sections for Negri bodies and examination of sections of different parts of the central nervous system, including the medulla, the ganglion nodosum of the vagus and sympathetic

<sup>3</sup> RIFKIN H., CHENADA, E. B., ZARROK, M., HENDERSON, D. G. & WHITEHEAD, J. O. The Diagnostic Significance of Inclusion Bodies in Rabies and Canine Distemper. *J. Lab. & Clin. Med.* 1945 Sept. 30 No. 9 748-51.

<sup>4</sup> RODRIGUEZ H. H. Sobre el diagnóstico histopatológico de la rabia. *Bolet. Inst. Bact. Chile* 1945 Oct., v 2, No. 3 111-39 3 figs. [23 refs.]

ganglia such as the stellate ganglion for the several infiltrative and degenerative lesions originally described by BABÈS (*Ann Inst Pasteur* 1892 v 6 209 and *C R Soc Biol* 1908 v 64 234) GOLGI (*Berlin Klin Woch* 1894 v 31 325) RAMON CAJAL and DALMARCO GARCIA (*Bull Inst Pasteur* 1905 v 3 298) and in nerve ganglia by VAN GEHUCHTEN & NELIS (*Ann Med Vet* 1900 v 49 243).

In all 200 cases were examined comparatively and it was reported to the author that rabies virus had been demonstrated by the inoculation of mice in 119 of these no virus was demonstrated in 81 instances. By the combined examination for Negri bodies in smears and sections and for the infiltrative and degenerative lesions rabies was diagnosed in 115 of the cases and negative results were recorded in four i.e. a percentage error judging by the mouse tests of 3 per cent. The percentage errors recorded were when the diagnosis was made by examination of smears alone for Negri bodies 27 per cent by examination of sections for Negri bodies 20 per cent. and by the combined examination of sections and smears for Negri bodies 15 per cent. The infiltrative and degenerative lesions were intense in 79 per cent. of cases and moderate in 21 per cent. Forty-eight of the cases reported to be negative by the histopathological methods were definitely so and thus was a percentage of 59 per cent of the 81 cases reported to be negative in the mouse tests. Thirty-seven were recorded as doubtful and four of these were diagnosed as rabies by inoculation of mice.

### (iii) Pathology

NEUJEAN<sup>\*</sup> reports that during the last three years he had to examine numerous dogs to determine whether they were infected with rabies. The procedure adopted which was considered very satisfactory was to inoculate suspensions of the brain into rabbits and mice and to examine sections for Negri bodies. He had been struck by the polymorphism of these bodies and the irregularity of their distribution. In addition the author noted the existence of small forms like dust dispersed outside the nerve cells among the nerve fibres and in certain cases ramified filamentous forms resembling a mycelium, which were difficult of interpretation.

He had been impressed by a suggestion of BRUMPT in 1938 in relation to the possible re-classification of the viruses of vaccinia and rabies which he now regards as prophetic. In view of these preliminary observations he tried culture methods which had been successful for growing rickettsia and he claims to have demonstrated the presence of the parasite of rabies by haemoculture. He describes the technique as being surprisingly simple. The blood from animals infected with rabies was collected in the presence of liquoide (Roche) [liquoide is described in the literature as a preparation of sodium polyanethol sulphonate for use in culture media to prevent coagulation and to abolish the bactericidal power of the blood]. In the beginning this blood was sown into two media Tyrode and Tyrode with 1/1000 agar. The examination of these media which had been sown with the blood suggested suspicious images only. However on examining the blood liquoide which remained after the sowing of the media he found an intense multiplication of corpuscles presenting all the characteristics morphology tinctorial affinity and structure of the corpuscles met with in rabies from anabistic bodies to noticeably vacuolated corpuscles and bodies usually called Negri bodies—from the limit of visibility to giant forms. Such multiplication was detected when the blood liquoide had been kept at about 25°C for 3 to 4 hours. Examination of the blood was carried out by taking a loopful and

<sup>\*</sup>NEUJEAN G. Mise en évidence par hémoculture du parasite de la rage. *Rec Trav Sci Méd Congo Belge* 1945 July No 4 139-41.

making smears which were stained by the May-Grünwald-Giemsa method or by Lestouard's method. The author states that the use of heparin or sodium citrate as anticoagulants appeared to hinder multiplication of the parasite which was found only with difficulty and showed profound morphological changes.

Positive haemocultures were recorded with blood samples collected in advanced stages of the disease from four rabbits infected with the Pasteur "fixed" strain of virus and from one rabbit and one dog inoculated with a street strain of virus. No attempt appears to have been made by the author to correlate the presence of the parasite with the infectivity of the blood for susceptible animals by intracerebral inoculation. He intends, however, to secure further information on the time of the appearance of the "corpuscles" in the blood in relation to the course of the disease and more convincing evidence may be forthcoming. [Confirmation of these observations is necessary. At this stage it is difficult to comment on what has not yet even reached the stage of being *sub judice*. The results reported would seem to be at variance with the irregular results reported in the literature in attempts to demonstrate the presence of the virus of rabies in the circulating blood but the methods employed up to the present may have been inadequate.]

#### (iv) *Methods of Treatment and Statistics*

CECCALDI<sup>6</sup> reports that two fixed virus strains are maintained by rabbit passage at Brazzaville. One is the Pasteur strain which was passaged 21 times during 1943 and the other is the strain "jeune chienne" of Brazzaville which was also passaged 21 times in 1943 and was in its 244th passage. Recently for the production of vaccine the Pasteur strain has been inoculated into sheep. This was necessitated by the shortage of rabbits and the need to produce relatively large quantities of vaccine. [A similar procedure has been forced on a number of other Institutes during the war period.] The virus is maintained entirely in rabbits: the sheep are inoculated for vaccine production only four times during the year. The vaccine up to November 1943 was prepared by the Semple method from 1 per cent. cerebral tissue with 0.05 per cent. carbolic acid, and was then changed so that the concentration of brain was 5 per cent. and of carbolic acid 1 per cent. The vaccine is considered to maintain its efficacy for a period of three months if kept in the cold. The opinion now held is that the rabies virus which occurs in French Equatorial Africa is normal in virulence and that bitten people should be treated by the same methods as those applied in Western Europe and other parts of Africa. Ten strains of street virus were recovered during the year: eight from biting dogs, one from a horse and one from a human being who died 21 days after the commencement of treatment 24 hours after a severe bite in the deltoid region. Negri bodies were demonstrated in the brain of the human patient and a street strain of virus was recovered. The case of the horse is described in detail but no history of a bite is given. Negri bodies were found in the horse's brain but they appeared to be infrequent and were small in size.

The chief interest in the report for 1943 by DURIEUX<sup>7</sup> of the activities of the Pasteur Institute in French West Africa is to be found in the observations on the results of vaccination of human beings against rabies since decentralization of the service was instituted in 1937. During the years 1938 to 1942, 1 122 patients were treated and four deaths occurred before the end of the

<sup>6</sup> BRAZZAVILLE [A. E. F.] RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1943 [CECCALDI, J. Director] 21-33. Page.

<sup>7</sup> AFRIQUE OCCIDENTALE FRANÇAISE. RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1943 [DURIEUX, C.] pp. 43-53. Service de la rage.

vaccine treatment. The decentralization would appear to be especially advantageous in cases of severe bites. Previously treatment was not commenced in some instances until 12 days after the bite. On the other hand decentralization when carried too far might have disadvantages. In outlying districts it is considered better to transport the patient to the centre where the vaccine is kept than to await the arrival of the vaccine which might lose activity in transit. The opinion is expressed that the dose of vaccine for children should be the same as for adults unless they are nurslings for whom it could be reduced slightly.

#### (v) Neuroparalytic accidents

KOENIGSFELD\* reports that a patient aged 43 years was bitten by a dog on 1st January 1944. Anti rabies vaccine treatment was commenced at once and 10 cc of vaccine was given over a period of 14 days. The vaccine prepared according to Semple's method consisted of a 5 per cent suspension of the brain of sheep infected with the Pasteur (Paris) strain of fixed virus. During the period of vaccination and contrary to advice the patient consumed alcohol but only in moderate amounts. Immediately after the last injection of vaccine the patient complained of severe headache pains and numbness in the thighs and arms blurred vision restlessness and complete insomnia. A retrobulbar neuritis of both eyes was detected and there was absence of abdominal reflexes. On 3rd February 1945 the patient was completely blind in both eyes but by the end of February his eyesight was almost normal. Recovery was recorded as complete by the first week of March. Vitamin B<sub>1</sub> 50 to 100 mgm. per day cod liver oil and liver extract had been administered. The author states that to his knowledge this is the first time that optic neuritis has been recorded in association with anti rabies vaccine treatment but the editor of the journal adds a footnote that he is aware of one other case not referred to in the literature in which an optic neuritis was ascribed to the effects of such treatment.

#### (vi) Miscellaneous

CASALS\* in a paper read to the American College of Physicians of New York gave a useful summary of the present state of knowledge with regard to rabies. He covered such points as the incidence of the disease in animals and man in America diagnostic methods prevention and control including vaccination methods. Much of the ground covered has already been referred to in recent reviews of American literature [this *Bulletin* 1943 v 40 200-202 269 653 655-6 1944 v 41 173 179-181 1945 v 42 170].

It is obvious that the author like many of his fellow countrymen considers that the incidence of rabies in the U.S.A. is a blot on their escutcheon. During a period of 15 years the number of cases of rabies in human beings has averaged 55 a year and from 1936-40 there were known to be at least 10 000 cases per annum in animals in the U.S.A. The continued potential danger is much greater than these figures might imply. He stresses the necessity of control of the disease in dogs by application of muzzling orders destruction of stray animals and strict quarantine orders. Such control he states is within the functions of the Public Health officials. [As already pointed out in the reviews on rabies in this *Bulletin* great headway is not likely to be made unless a uniform policy for the control of the disease in the whole of the U.S.A. is adopted this

\* KOENIGSFELD E G H Neuroparalytic Accident following Anti Rabies Vaccination. *J Roy Army Med Corps* 1945 Nov v 85 No 5 254-5  
 \* CASALS J A Current View of the Rabies Problem. *Ann Intern Med* 1945 July v 23 No 1 74-8.

control to be in the hands of the Bureau of Animal Industry who would have to have the co-operation of the police. The Public Health authorities would take the necessary measures with regard to treatment of human beings. The reviewer understands that this could only be effected by altering the Laws of Congress, but surely this is not an insurmountable difficulty. At present each State has its own policy of control, and in most cases the police apparently believe that responsibility for control lies with public health officials only.] CASALS<sup>18</sup> states that Australia is kept free of disease by enforcement of quarantine laws. He is not accurate when he says that in England relaxation of the ordinances on muzzling and leashing has been found to result in a sharp increase in the number of cases of rabies, as can be confirmed by reference to the last review on rabies [this *Bulletin* 1945 v 42, 680-682]. [Great Britain like Australia, is favourably placed geographically with regard to control of the disease and the regulations in force require all canines and felines landed in Great Britain from abroad to be quarantined for a period of six calendar months after landing on premises approved by the Ministry of Agriculture. Outside quarantine kennels no cases have been confirmed since 1922, and the disease is likely to be introduced only by criminal evasion of the quarantine regulations. Only when the occurrence of the disease outside kennels was confirmed would muzzling and leashing orders be applied.]

HABEL<sup>19</sup> in his very comprehensive paper recording the results of well controlled experiments in guinea-pigs, mice and monkeys strongly suggests that further consideration should be given to seroprophylaxis either alone or combined with vaccine in anti-rabies treatment. As he points out, seroprophylaxis in rabies should theoretically be highly effective provided protection is in part or entirely due to circulating antibodies since the time of exposure to infection is known, and the incubation period is often prolonged sufficiently for active immunity to be produced before the virus has established itself in the vital centres in the C.N.S. Yet in the U.S.A. little attention has been given to this method of prevention. The author has reviewed some of the earlier work on anti-rabies serum in which conflicting results were obtained, but the experiments were made on only a few experimental animals and were inadequately controlled. During more recent years from 1934 to 1939 workers notably in Rumania and India [see this *Bulletin* 1934 v 31 642 1935 v 32, 180 610-612 1937 v 34 235 1938 v 35 173 1939 v 36 727] have considered the question of serum prophylaxis in rabies

have carried out experiments in guinea-pigs, rabbits and monkeys to test the effect of anti-rabies serum. These same workers have also reported on the use in man of serum alone and serum combined with vaccine. The present author by applying more recent methods of testing the potencies of virus, antiserum and vaccine has extended these observations and presented the problem in a new light. His main conclusion, which would appear to be well justified, is that his experimental results in animals warrant a trial of immune serum either alone or combined with vaccine in prophylactic treatment of the disease in man. He makes suggestions for the application of serum prophylaxis based on the results of his experiments which differ from anything that has been tried before, viz (1) Anti rabies serum alone would be administered in those cases of infection now requiring only 14 doses of vaccine i.e. cases of doubtful infection (2) immune serum followed by commencement of a course of vaccine treatment 6 days later in those cases now requiring 21 doses of vaccine. It is known that a large number of people at present receiving vaccine treatment against rabies have not definitely had an exposure to virus infection and they

<sup>18</sup> HABEL, K. Seroprophylaxis in Experimental Rabies. *Pub Health Rep* Wash. 1945 May 18 v 60 No 20 645-60 3 figs. [34 refs.]

are thus exposed to the discomfort and in some cases possible unpleasant sequelae of vaccine treatment. This has been considered necessary as early treatment is indicated and diagnosis of the disease in the biting animal is not always definite. However by employing mice for the diagnosis of the disease in the biting animal it is now possible to get a reliable answer to the diagnostic test in 6 days. If the result is negative no vaccine need be given and the patient would have only had one dose of serum. On the other hand if the result is positive vaccine treatment would be commenced. In the latter case the serum could act in two ways by local destruction of the virus and by retarding the spread of the virus in the CNS as evidenced by the present experiments in which the incubation period was prolonged even although the animals did not prove to be completely protected. This prolongation of the incubation period is probably just what is required for the vaccine to be effective (it would appear that in many failures in vaccine treatment the incubation period is short) hence the better results in the animal experiments with a street strain of virus when serum and vaccine treatment were combined with an appropriate interval of 6 days between the two. The use of serum locally at the site makes possible specific treatment while the virus is localized. The author describes a method for the preparation of an anti rabies serum and concentration of the antibodies and no doubt this could even be improved upon. It would be impossible to discuss all the details of the author's experiments in a short review.

Ian A Gallaway

BARANOVSKAYA S A [Prolonged Passage of Rabies Street Virus in White Mice.] *Zhurnal Mikrobiologii Epidemiologii i Immunobiologii* Moscow 1943 No 12 76-8 [In Russian.]

LEGEZYNSKI [this *Bulletin* 1939 v 36 725] has stated that street virus and fixed virus behave differently on serial passage in white mice in that the former could only be passed 4-6 times while fixed virus went through 56 passages without loss of virulence and that this difference was sufficiently constant to be used as a means of differentiating between the strains.

In the course of routine passage of various strains of street virus in white mice the author has accumulated data which are in opposition to the findings of Legezynski. Twenty cases of passage from human dog and bovine brains to white mice are reported the virus could be taken through 10-30 passages without loss of virulence while the incubation period soon fell to 5-7 days. Only in one case did the virus die out in the fourth passage. It is suggested that the difference between these results and those of Legezynski may be due to the fact that the latter was dealing with less virulent West European strains.

D J Bauer

MCDONALD S A Method for the Demonstration of Negri Bodies. *Indian J Med Res* 1944 Oct. v 32 No 2 205

- 1 Fix thin slices of *hippocampus* and *cerebellum* in 10 per cent formol saline for 24 hours and prepare paraffin sections in the usual manner
2. Take sections to tap-water
- 3 Stain with Weigert's iron haematoxylin for 10 minutes
- 4 Rinse in water and transfer to Masson's ponceau 2R-acid fuchsin diluted 1:10 with distilled water for 5 minutes

Stock —Ponceau 2R	0.7 g
Acid fuchsin	0.35 g
Glacial acetic acid	1.0 cc.
Aq. dest.	100.0 cc.



the muscles of his back, and after eight or nine weeks he was able to sit alone. He was given daily hydrotherapy treatment, massages and so on for about two months. His progress has been slow but steady. He can now walk without crutches and can hold light things in his hands. At present he is taking 30 mg of thiamine daily and swimming three or four times a week. In the past month he has been able to take a light job. Perhaps he is one of a group who would have got well eventually regardless of what was done even though he was getting steadily worse until treatment was instituted.

REMLINGER, P. Los fracasos del tratamiento antorrábico (Accidents in the Treatment of Rabies. *Rev Sanidad e Hig Pública* 1945 Sept v 19 No 9 589-67

MULLETT C F. Hydrophobia. Its History in England to 1800. *Bull. History of Med* 1945 June 18, No 1 44-65. Refs in footnotes.

## MALARIA

PESET ALEXANDRE, T & ROMEO VIAMONTE, J M. Estudio de las mareas del Guadalupe desde el punto de vista de su endemia palúdica. [A Study of the Country round the Lower Reaches of the Guadalupe in relation to Endemic Malaria.] *Rev Sanidad e Hig Pública* 1945 Oct v 19 No 10 687-700 2 graphs.

ACKERKNECHT E H. Malaria in the Upper Mississippi Valley 1780-1900

This book is reviewed on p 281

RUSSELL, P F, RAO T R & PUTNAM, P. An Evaluation of various Measures of *Anopheles* Larva Density. *Amer J Hyg* 1945 Nov v 42, No. 3 274-98 9 figs

"Various expressions of *Anopheles* larva density have been computed by simple and by partial correlation technique. The data were collected in a survey covering 33 months, from June 1937 through February 1940 in Pat tuklotta Town and Taluk Tempore District, Madras Presidency, India, a recently opened rice field area where *A. culicifacies* is a prolific breeder as well as the malaria vector. The analysis was applied to data pertaining to larvae of this species and to those for all *Anopheles* larvae captured in the area. It has been shown that

"1. Good correlation exists between the logarithms of the monthly captures and either collection unit minutes or square feet. The relationship is, therefore exponential in character

"2. When regression equations expressing the relationship between larvae captured and both minutes and square feet are computed, the minutes spent dipping are found to be the determining factor. Area covered does not contribute to the number of larvae captured when time is held constant. Captures in wells during 1937 and in borrow pits throughout the period are exceptions to this rule.

"3. The precise form of the equation describing the relationship differs for larvae captured from different habitats. It also changes from one year to another

"4. For routine field use a simple ratio of larvae captured to minutes spent dipping furnishes a practicable measure of density"

ROMEO VIAMONTE, J. M. & IRIGOYEN RAMIREZ A. Nota previa sobre el anofelismo de la Zona del Protectorado español de Marruecos. [Anophelines of Spanish Morocco] *Rev. Sanidad e Hig. Pública* 1945 Oct. v 19 No 10 669-74 3 figs. on 1 pl. & 2 graphs.

MOHAN B. N. Details of the Procedure adopted in maintaining a Laboratory Colony of *A. fluviatilis*. *J. Malaria Inst. of India* 1945 June v 6 No 1 75-6

Since January 1944 a colony of *Anopheles fluviatilis* has been maintained at Mettupalaiyam seventeen miles east of Coonoor.

It was started from eggs obtained from wild-caught females which were isolated in tubes containing damp filter paper. The eggs were floated in waxed cork rings on water in mud-lined enamel bowls. For larval food hay infusion was added to the water together with brewer's yeast or (when obtainable) a mixture of litmus milk (2 parts) and dehydrated blood serum (1 part). The water was aerated daily. Newly formed pupae were removed to bowls of clean water in a colony cage (2x2x2 feet) which was kept inside a larger one.

Humidity in the cage was maintained by hanging up damp cloths and providing a screened tray of saturated solution of common salt. For the adults glucose water on cotton wool was available and a rabbit with shaven back was put in the cage every night. The bred adults paired only in the presence of a blue light. The females laid their eggs on the water in mud-lined bowls and earthenware pots—more in the pots than in the bowls.

Though the colony now appears to be flourishing it was observed that the females fed more readily on the rabbit after several egg layings. It is therefore important that such a colony should be allowed to become well stocked and established before removing any mosquitoes for experimentation.

H. S. Leeson

KEENER G. G. Jr. Detailed Observations on the Life History of *Anopheles quadrimaculatus*. *J. National Malaria Soc. Tallahassee, Fla.* 1945 Sept. v 4 No 3 263-70 3 figs.

The author worked with a large colony of *Anopheles quadrimaculatus* kept in cages in an institution in Alabama and maintained under nearly constant climatic conditions (high humidity, air 76° to 80°F, water about 4° lower).

The paper contains a large amount of fact, some of it not easy to summarize. Males and females emerge in approximately equal numbers, the males before the females—as in many other mosquitoes. The author gives information about the average duration of the early stages including the separate larval instars. The time from laying of egg to emergence of adult is a mean of 21 days and particulars for the duration of the several instars are given. As to the length of life of the female it seems that 50 per cent. of them survive 21 days and the maximum is given as 62 days but there are no particulars as to how they were fed whether they were mated and so forth. Pairing takes place most commonly at about 8 p.m. (season and natural illumination not stated) the insects being then extremely active. The female can pair either before or after a blood meal and can then lay several batches of fertile eggs though there is no statement as to whether fertility falls off gradually after a single pairing. The insect takes about 3 cmm. of blood at a meal and during the first few days of life occasionally feeds more than once in the 24 hours. The female deposits eggs while she is standing on the side of the bowl close to the edge of the water, the eggs appearing at the tip of the abdomen and being jerked off into the water singly at intervals of a few seconds. Five females

[March, 1948]

were kept singly and averaged over 200 eggs per batch some of them laying nine to twelve batches a figure which does not seem consistent with the statement that the insect may produce three to four thousand eggs.

The paper contains a large amount of valuable information the quantitative material would have been more useful if the author had given original figures rather than percentages and some indication of the consistency of results. All who have maintained colonies of *Anopheles* know that the differences between successive experiments are often great

P A Buxton

METCALF R. L. The Physiology of the Salivary Glands of *Anopheles quadrimaculatus* J National Malaria Soc Tallahassee Fla 1945 Sept. v 4 No 3 271-8

The author presents information on the anticoagulins and agglutinins in the salivary glands of *A. quadrimaculatus*.

Anatomically the glands resemble those of other species of *Anopheles* with two lateral acini and one median acinus which is shorter. The lateral and median acini differ in the type of gland cell, and in the pH of the crushed acinus (lateral about 6 median about 7). The ducts including those inside the acini are lined with chitin (identified only by a blue violet fluorescence).

The crushed whole gland of the female mosquito contains an agglutinin this is much stronger in the median than the lateral acinus and develops when the insect is a few hours old. It is active even at one in a million, on corpuscles of many sorts of mammal including men of several blood groups but is not active on chicken or turtle blood. The glands of the female also contain an anticoagulin active at dilutions of one in ten thousand. The agglutinin and anticoagulin are thermostable.

Females of other species of *Anopheles* examined by the authors and by other workers contain essentially similar salivary agglutinins and anticoagulins. Females of a number of *Culiseta* contain neither. Males of *A. quadrimaculatus* contain neither.

The glands of female *A. quadrimaculatus* appear to contain no digestive enzymes protease lipase and amylase could not be demonstrated

P A Buxton

BRADLEY G H & FRITZ R. F. Observations on Seasonal Occurrence and Abundance of *Anopheles quadrimaculatus* Say J National Malaria Soc Tallahassee Fla. 1945 Sept v 4 No 3 251-62, 12 figs

The authors have tabulated a very large amount of fact on adult *Anopheles quadrimaculatus* in the U.S.A. particularly the South and East. They are concerned mainly with the season in which adults occur in catching stations and with their numbers. Data are graphed against average annual temperature and the county is divided into zones at 5°F intervals. In the warmest zone (70-75°F) the peninsular Florida southern Texas and Louisiana) adults occur all through the year and the same is almost true in the 65-70°F zone. In the third zone (60-65°F) there is a definite absence of adults from houses during the four winter months and this period is longer in the next two isothermal zones. The maximum number which may be taken in a catching station is not apparently very different in the five zones maxima at the peak month run from about 1 000 to 5 000 per catching station. In the colder parts of the country with annual means below 50°F no "significant" numbers of this insect are recorded. [As a rough way of tabulating a large amount of information the method seems to justify itself.]

P A Buxton

EYLES D E, SABROSKY C W & RUSSELL J C Long-Range Dispersal of *Anopheles quadrimaculatus* *Pub Health Rep Wash* 1945 Oct 26 v 60, No 43 1265-73 3 figs. (2 on pls.)

The authors have investigated the range of flight of *Anopheles quadrimaculatus* round a certain very large breeding place in South Carolina. Circumstances were unusual and marked mosquitoes were frequently recovered over two miles from the release point the extreme figure was 3.63 miles measured of course in a straight line

The paper is full and well recorded (though the map has no scale) Some 3 500 mosquitoes marked with aluminium powder were released at one point on a single day in the centre of a very large swamp Owing to the extent of the swamp there were no catching stations or domestic animals within two miles. In all 21 of the marked mosquitoes were recovered (in some 40 000 caught and examined) The authors point out that even within one species of mosquito range of flight is influenced by a great variety of factors. They do not regard these observations as contradictory to the generally held view that a one-mile limit of control is generally satisfactory for *A. quadrimaculatus* They conclude that areas must be studied individually [For a similar experiment with *A. quadrimaculatus* in Delaware see this *Bulletin* 1945 v 42 687] P A Buxton

CAUSEY O R, DEANE L M & DEANE M P *Anopheles aquasalis* vs *Anopheles tarsimaculatus* as the Name for the Brackish Water Anopheline of Central and South America and the Caribbean Islands *J National Malaria Soc Tallahassee Fla.* 1945 Sept. v 4 No 3 243-50 [18 refs.]

MILES V I Differentiating the Larvae of *Anopheles georgianus* King, *A. bradleyi* King and *A. punctipennis* (Say) *J National Malaria Soc Tallahassee Fla.* 1945 Sept. v 4 No 3 235-42, 3 figs.

CASTILLO Roberto Levi Los anofelinos de la Republica del Ecuador Vol 1 This book is reviewed on p 262.

SCHULTES W Bedeutung der Sternalpunktion in Diagnose und Rezidivprognose der Malaria. [The Value of Sternal Puncture for Diagnosis and Prognosis in Malaria.] *Munch med Woch* 1944 July 28 v 91 Nos 29/30 384-5

Sternal puncture is a valuable means of diagnosis in chronic malaria when parasites cannot be found in the blood or only after repeated examinations by its use the author found trophozoites in 66 (51.5 per cent) of 128 cases of clinical malaria in soldiers. It is also useful for prognosis as regards the likelihood of the occurrence of relapses and for judging the fitness of soldiers for active service after recovering from an attack of malaria. A further 176 patients soldiers, were examined by sternal puncture after a course of atabrin [mepacrine] and plasmoquine [pamaquin] no plasmodia were found in 79 ring forms and dividing forms were present in 7 (they had no fever) half grown and fully-grown parasites were found in 78 and gametocytes only in 12. In these cases no parasites were found in blood films.

The technique is simple and causes little pain but experience is needed in the microscopical examination of the marrow preparations J F Corson

BOOKLESS A S & NAFTALIN J M Typhoid Fever complicated by Benign Tertian Malaria. *Brit Med J* 1945 Dec 8 804-5 1 graph.

The authors have had under their observation recently 34 cases of typhoid fever in two of which benign tertian malaria preceded by 17 days the onset

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### Tropical Diseases Review

of typhoid and in ten where the two infections were present together. The cases were part of two small outbreaks, and among the first 4 patients P. vivax was found in the blood of two, but none received antimalarial treatment [our team, in two only "did the temperature charts suggest double infection showing alternating fevers and remittent fever for the first four days." In where the fever at the onset was irregularly remittent]. The interest of this paper lies in the patients with concurrent infections of malaria and typhoid fever. There were, as stated already, ten such, and the course in four was mild, in three "moderate" and in three only was it severe (there were no fatalities among these and only one patient had a relapse (not malaria). These figures are to be contrasted with the 24 plain typhoid cases of which 12 were mild, 8 "moderate" 3 severe and 3 fatal 8 cases relapsed. It was noted that antimalarial drugs did not form an obstacle to positive haemoculture for *B. typhosum*. This was positive for 28 out of the total 44 cases. It is noteworthy also that "O and VI agglutination tests were not carried out systematically. Thirdly patients with uncomplicated B.T. malaria always improved on quinine," state the authors. In the early stages of illness indications of so serious a disease as typhoid fever were absent, and the early diagnosis on clinical grounds was hindered [the authors term] by the simultaneous presence of or immediate recovery from malaria.

[It is to be hoped that more of these cases will be reported, and many are likely to occur. The reviewer noted all the above facts 28 years ago (Ann. Trop. Med. & Parasit. 1919 v 13 185-214 this Bulletin 1920 v 15 252)] but they seem to have been forgotten. Sir Patrick Maxwell had noted earlier still that in malarious subjects the onset of typhoid is often preceded by three or four paroxysms exactly like those of ordinary ague and that the failure of response to quinine should put us on our guard. It is—it certainly was—regrettably far from uncommon for the tropical practitioner to give quinine to any patient with fever and only when fever continued in spite of the quinine did he begin to look for causes other than malaria. Again, any disease pneumonia for example, in a malarious subject is apt to assume an intermittent or periodic character. Sometimes, as SCOTT has recorded (*ibid*) the temperature chart may be that of straight malaria, but clinical signs of typhoid fever—rose spots, pea-soup stools etc.—may be quite in evidence. The fact that no fatalities occurred among the authors' patients with the dual infection, and that 7 of the 10 were mild or moderate corroborates the conclusion in the paper referred to above, that cases of coincident enteric fever and malaria (even though each disease by itself is serious) often run a remarkably mild course. Incidentally reference may be made to the remark of Sir Abner Wright of his having observed that antityphoid inoculation appeared to reduce the susceptibility to malaria. The subject of the antagonism of diseases is a very fascinating one and too little work has been done upon it. An interesting thesis, even a whole book, might profitably be written on the question.]

H. Harold Scott

GELFAND M. Malaria in the European and in the African Patient. *Clin. Proc.* Cape Town. 1945 Sept., v 4, No 7 421-9

PERRET-GENTIL, A. Essais de traitement de la malaria tertiana par la Vitaquine. [Treatment of Malaria with Vitaquin.] *Paris. Berne.* 1945 Juh 5 v 34 No. 27 402-5 3 charts. [13 refs.]

Vitaquine is a mixture of cinchona alkaloids, 40 per cent. of which are sulphates of quinine and hydroquinone with a vitamin C preparation, Redoxo "Roche". Each tablet contains 0.2 gm. of the sulphates of cinchona alkaloids and 0.05 gm. of ascorbic acid. Twenty-five refugees suffering from

relapsing *P. vivax* malaria in Switzerland were treated with this preparation. A course of treatment consisted in the administration of 2 tablets three times a day at meal times for 5 days. After an interval of 3 days the course was repeated. Five or more such courses were given to some patients. Parasites disappeared from the blood on the 3rd or 4th day and the general condition of the patients improved. A certain amount of gastric irritation in some patients was relieved with colloidal aluminum hydrate or belladonna preparations. As the urine of most of these patients originally gave a negative reaction with dichlorophenol indophenol which was rectified by treatment the administration of vitamin C appeared to be beneficial.

Norman White

VOLLNER H & LIEBIG H Nebenwirkungen des Atebrins am Zentralnervensystem. [Side Effects of Atebrin on the Central Nervous System] *Deut med Woch* 1944 July 21 v 70 Nos. 29/30 415-17 [12 refs.]

The author refers to GELLER's conclusions [this *Bulletin* 1945 v 42 9] with which he disagrees and records four cases of benign tertian malaria in which attacks of mania and in one case temporary paralysis were apparently caused by atebrin injected intramuscularly.

The first patient had five attacks of malaria in four months the second third and fourth of which were treated with quinoplasquine and no nervous disturbances occurred. In the first attack atebrin was given in doses of 0.3 gm i.m. daily for 3 days and 0.1 gm. orally *t.i.d.* for the next 4 days after the second injection the patient showed mild maniacal excitement and at the end of the oral course he had a severe maniacal attack which began suddenly and lasted for nearly three weeks. In his fifth attack of malaria mild mental disturbance followed the second injection of atebrin.

The second patient also had five attacks of malaria within a few months and all were treated with atebrin and plasmoquine. In the first second and fourth attacks there were no nervous symptoms but in the third attack the third injection of atebrin [presumably 0.3 gm.] was followed by the development of cramps numbness and paraesthesia in the legs. His fifth attack of malaria was treated with double doses of atebrin—0.3 gm i.m. *bis die* for two days then 0.6 gm. orally for 5 days. In the night following the fourth injection the patient became acutely maniacal four men being required to restrain him. On the following day he had hiccups laryngeal paralysis and flaccid paralysis of the legs with diminished deep reflexes. He recovered quickly from the mania but the paralysis lasted for about ten days.

The third patient was treated for his first attack of malaria with double doses of atebrin—0.3 gm i.m. *bis die* for three days. In the night following the third day he got out of bed ran across a yard barefooted to the office and demanded to be shot dead immediately. A few minutes later he became violently delirious requiring eight men to hold him. No other neurological symptoms developed.

The fourth patient had three attacks of malaria in three months. The first two attacks were treated with atebrin 0.3 gm i.m. daily for three days then 0.1 gm orally *t.i.d.* for 4 days and no nervous symptoms developed. His third attack was treated with double doses—0.3 gm i.m. *bis die* for two days. In the next night but one after the last injection he wandered aimlessly about the hospital. Treatment with atebrin 0.6 gm. daily by mouth was continued Luminal [phenobarbitone] being also given and there were no further mental disturbances.

The authors add that such attacks are rare the first patient was one among 350 treated with the usual daily dose of 0.3 gm of atebrin but the other three were among over 100 patients treated with double daily doses. Treatment

was not interrupted but was continued by oral administration and the authors think that their results justify this decision. [See also this *Bulletin* 1945 v 42, 253-343 and 685.]  
J. F. Corson

ZELIGS M. A. The Management of Chronic Malaria between Attacks, with special reference to the Effect of Nicotinic Acid on Malarial Headache. *J Amer Med Ass* 1945 Nov 17 v 129 No 12, 796-8.

Many members of the fighting services contracted malaria while in actual combat against the enemy. Chills and fever were an accompaniment of battle weariness, hunger, intense fear and exposure to wet and cold. After removal of such patients from the field, the febrile attacks could be readily cured, but symptoms such as easy fatigability, irritability, loss of weight, headache, backache and disturbed sleep were liable to persist. This condition was often described as "post-malarial asthenia." The description is not apt. Malaria may play a part in the causation of the condition but so do the physical and psychological stresses of combat, and possibly also other tropical infections such as amoebiasis and ankylostomiasis. After return to the United States and three months of reconditioning, malaria infections may persist but "asthenia" is very rare. The term "post-malarial asthenia" should be abandoned.

There are, however, certain symptoms so constantly associated with chronic malaria as to incriminate the malaria parasite as the cause. Most common of these is malarial headache. This headache is usually bifrontal, mild to moderate in severity, never hemispherical, has no neurological prodromes, occurs on rising in the morning and usually improves after the patient has been up for a few hours. Prolonged persistence of malarial headache may produce secondary "neurotic-like" phenomena. The sufferers are not relieved by the usual headache remedies. Twenty-five selected patients were treated with nicotinic acid, 100 mgm. by mouth. The headache was relieved in 10 cases; there was moderate improvement in seven cases and no improvement in eight. No parasites were found in the blood and there is no record of antimalarial treatment.  
Norman White

RUPPOZ, A. Paludisme, enfance noire et quinquisation au Cercle de Gombo-Matadi en 1938-1939. [Malaria, Native Children and Quinquisation in the Gombo-Matadi Region of the Belgian Congo in 1938-1939.] *Rec Trav. Sci. Méd. Congo Belge* 1945 July No. 4, 82-9.

In 1938 the author examined thick smear blood preparations taken from a number of children in three villages that had previously been outside the range of activity of any medical organization. The children were considered in the villages to be enjoying normal states of health, though a child without an enlarged spleen was very exceptional. In 1939 infant welfare centres were at work and infants were given prophylactic quinine 0.25 gm. four times a week. In that year the blood of all infants who were ill and who needed medical treatment was examined. The results of the blood examinations in the two years are given in detail and compared. In 1938 the blood of 16 out of 17 infants below the age of 6 months and of all older children up to 5 years, contained malaria parasites. *P. vivax* was rare. *P. falciparum* and *P. malariae* were both abundant. The *P. falciparum* gametocyte index of these infants up to 5 years was 52 per cent., the *P. malariae* gametocyte index 54 per cent., the *P. vivax* gametocyte index 4 per cent. Mixed infections were common. In 1939 the parasite index was but little reduced, but the parasite density was markedly less. The gametocyte index was 50 per cent. lower mixed

infections were rare and quartan infections were much fewer except during the first six months of life. These improvements are attributed to the distribution of prophylactic quinine

Norman White

PHILIP M I RAMAKRISHNA V & RAO V V Turmeric and Vegetable Oils as Repellents against Anopheline Mosquitoes. *Indian Med Gaz* 1945 July 1 80 No 7 343-4

The authors have observed that in the Jaypore hill tracts and on the Madras coast spleen rates in boys are much higher than in girls. They think that this must be due to girls being less bitten by *Anopheles* than boys and therefore less infected with malaria. This in turn is attributed to the fact that girls and women apply turmeric and vegetable oils to their bodies daily. In cage experiments an application of turmeric and mustard oil subsequently washed with water but without soap is repellent to hungry *Anopheles* of several species.

[It is one thing to repel in a cage experiment quite another to find some thing which will remain even moderately repellent after rubbing on garments and for several hours]

P A Burton

MEDICAL ADVISORY DIVISION HEADQUARTERS SUPREME ALLIED COMMAND SOUTH EAST ASIA. Trials of Malaria Control in South East Asia. Second Introductory Report. Indoor Spraying with D.D.T. 3 mimeographed pp 2 figs. [Undated.] D.D.T. Report, No 5 Indoor Spraying with D.D.T. [SCHARFF J W Colonel Med Adv Div SAC SEA] 51 mimeographed pp 2 photos. [Dated 23rd Oct 1944] D.D.T. Report No 6 D.D.T. Air Spray Trial at the R.A.F. Station, Jessore September, 1944 [SCHARFF J W Colonel with Senior WHITE Major I.A.R.O. (Med.)] 8 mimeographed pp 1 plan. [Dated 23rd November 1944] D.D.T. Report No 7 Third Introductory Report. Air Spray Trials, Tamu Area, October, 1944 [Entomological data furnished by MACAN T T Major R.A.M.C. Summary prepared by LAMBERT J D Major R.E.] 3 mimeographed pp 2 figs. [Dated 23rd November 1944]

These papers constitute between them a lengthy report on the early trials with DDT in the Far Eastern theatre of war to test its value in the control of mosquitoes both adult and larval for the protection of troops against malaria. All the trials were of the field type. For destruction of adult mosquitoes a 5 per cent. solution of DDT was applied usually by means of a power driven sprayer of the paint spray type the average dose of DDT per square foot of wall surface was 56 mgm the huts treated were both thatch and of permanent construction and the mosquitoes concerned were *Anopheles subpictus* *A. annularis* *A. hyrcanus* *A. culicifacies* and *A. pallidus*. The normal procedure was to select a suitable group of houses and to establish catching stations in them in which periodical mosquito counts were made all dwellings were then sprayed the catching stations being reserved to the last and counts were continued in the treated catching stations.

Catching stations were of two types—netted and un netted. The former were completely open at night but were closed by an arrangement of mosquito netting at dawn thus imprisoning any mosquitoes in them they remained closed for some hours until the count was made. It was intended by this means to avoid errors due to the early morning migration of mosquitoes though it was recognized that the method held them artificially in contact with treated surfaces from which they might otherwise have been repelled. The un netted stations were ordinary open houses in which hand collections



were made some hours after dawn. Curiously and for reasons not understood, the catches in the two types of stations were the reverse of what had been expected, being higher in the un-netted stations, from which the mosquitoes had an opportunity of escape than from the netted ones.

An almost complete disappearance of mosquitoes was recorded during the month after DDT treatment after which there was a steady increase in anophelines in un-netted stations though the numbers previously found were not reached for several months. The results were better when every habitation within the area was treated. DDT exerted no repellent effect, but there was some inhibition of biting in rooms which had recently been treated, and it was found that *Culex fatigans* was more resistant than *A. subpictus*.

The various types of equipment which might be used for distribution of residual films were surveyed, and it was concluded that the "Kent" pattern (a pneumatic knapsack machine in the body of which a high pressure is initially obtained by means of a hand pump) was suitable, though it needed some modification. The technique of application is described.

Larval mosquito control was carried out from the air using Hurricane aircraft equipped with two tanks, each holding 250 pounds of 5 per cent. solution of DDT in kerosene and application was at the rate of two to three quarts per acre. Some of the applications were made from formation flights of several aircraft in line abreast. Complete immediate control of swamp-breeding anophelines (*A. hyrcanus* and *A. philippinensis*) was secured. Fully developed larvae did not re-appear for about 12 days after treatment and this result was associated with a marked reduction in the adult mosquito prevalence in the neighbourhood. When the same method was applied to country in which streams, containing larvae of such species as *A. minimus* abounded, full destruction of larvae was not secured, owing to the shielding effect of overhanging vegetation. Nevertheless, the DDT remaining on this vegetation killed mosquitoes coming to lay or newly hatched, and in consequence very effective control of adults was secured despite the incomplete larvicidal result.

G. Macdonald

AFRIDI, M. H. & ARTHUR, J. H. Future Military Malaria Control. *South African Med J.* 1945 Oct 13 v. 49 No. 19 361-5 2 charts & 1 map.

The title of this paper "future military malaria control," is not really applicable to the subject matter which consists of an account of the incidence of malaria and the measures taken for its control on the Indo-Burma front during the years 1942 to 1944. Very high malaria rates were experienced in the first part of the campaign, though even then the control measures adopted were instrumental in avoiding a complete breakdown such as occurred in some areas where they were neglected. The anophelines incriminated as carriers were *Anopheles minimus*, *A. pyreticus* var. *caudatus*, *A. leucophrys*, *A. soudanicus* and *A. philippinensis* one or more of which occurred in considerable numbers in most areas and almost throughout the year. The seasonal prevalence of each is shown in a useful histogram.

Drainage was considered to be the backbone of control though adult destruction and larvicides were also used. But despite these and a carefully organized system which covered the whole line of communications the incidence of malaria remained high, the chief incidence being among forward troops, to whom suppressive treatment had been given from the first. Failures in control among these troops were due to neglect to take mepacrine when on patrol when they were away from the supervised parades at which it was administered, to reluctance to use head nets which obstructed vision, and to dislike for and inefficiency of the original repellent cream, or even the later pyrethrum

creams and dimethyl phthallate. These last objections were finally overcome by the adoption of a  $\frac{1}{8}$  in. mesh net which when impregnated with dimethyl phthallate afforded complete protection against mosquito bites for 72 hours while following the Australian demonstration of the efficacy of mepacrine an educational campaign resulted in the growth of greater faith in it and its more regular use.

Also in the later part of the campaign DDT became available and this was particularly valuable when applied from the air for the control of breeding places made difficult of access by jungle or by enemy mines.

The authors consider that the introduction of DDT and the use of mepacrine and repellent fish nets stand out pre-eminently as advances in malaria control which they will profoundly influence in the future

G Macdonald

LOZANO MORALES A Problemas prácticos de lucha antipalúdica. Estudio experimental de un nuevo larvicida [Practical Antimalarial Problems Experimental Study of a New Larvicide.] *Rev Sanidad e Hig Pública* 1945 June v 19 No 6 413-24

*Exadoruro de benceno* [benzene hexachloride or hexachlorocyclohexane  $C_6H_6Cl_6$ ] is a white powdery substance insoluble in water. It was synthesized in England as long ago as 1820 but only recently have its insecticidal properties been recognized. The author has demonstrated its value as a larvicide. Laboratory and field experiments are described. Excellent results were obtained by the application of the powder 1 per cent mixed with road dust to *Anopheles* breeding places. Suspensions in water following Barber's method of distributing Paris green also gave good results. Norman White

HENDERSON J M Antimalaria Measures for the Protection of Military Personnel in Puerto Rico and their Applicability to Civilian Malaria Control. *Puerto Rico J Pub Health & Trop Med* 1945 June v 20 No 4 419-45 6 charts & 1 fig [Spanish version 446-72.]

COULSTON I, CANTRELL, W & HUFF C G The Distribution and Localization of Sporozoites and Pre-Erythrocyte Stages in Infections with *Plasmodium gallinaceum*. *J Infect Dis* 1945 May-June v 76 No 3 226-38 [14 refs.]

In a previous paper [this *Bulletin* 1945 v 42 538] two of the authors described the development of sporozoites of *P. gallinaceum* in the skin and organs of chickens following cutaneous and intravenous inoculations. In the present paper are recorded the results of the inoculation into uninfected birds of blood and of organ or tissue emulsions of infected birds at varying intervals after the latter had received an injection by mosquito bite or by syringe of sporozoites. In chickens bitten by infected *Aedes aegypti* none of the organs or the blood were infective during the first 36 hours. The muscles at the site of the bite were, however, infective. From the 36th to the 79th hours occasional infections were produced by the blood and some organs (lung spleen heart). After the 79th hour the blood and organs regularly produced infections. After intravenous injection of large numbers of sporozoites the lungs spleen kidneys liver pancreas and muscle produced infections during the first 36 hours. The blood was infective at the 36th hour but was negative thereafter till the 82nd hour. At the 70th hour all tissues became infective. When suspensions of sporozoites from 130-200 mosquitoes were inoculated intravenously the presence of sporozoites in the blood was demonstrated for 5 to 20 minutes by subinoculation and up to 15 minutes microscopically.

Subsequently the blood was negative till 40 hours later. Infected mosquitoes were allowed to bite the tip of a chicken's wing. The tip was isolated by ligature after varying intervals and then removed. Even when only 45 seconds had elapsed before the ligature was applied, the birds became infected. In practically all cases the removed portion of wing produced infection when subinoculated to uninfected chickens. The result indicates that dispersal of sporozoites probably takes place by way of the blood stream. [These results may be compared with those observed in man by FAIRLEY and his colleagues see this *Bulletin* 1945 v 42, 630.] C. M. Wemyss

JACOBS H. R. Immunization against Malaria. Unsuccessful Attempts to Increase Resistance of Ducklings to *Plasmodium lophurae* Infections by previous Injections of Materials containing the Forssman Antigen. *Amer J Trop Med* 1945 Mar v 25 No 2, 151-3.

In a survey of animals susceptible to malaria it was noted that those possessing Forssman antigen or hapten are generally not liable to malaria infection. In most animals the hapten when present occurs in the tissues but in the sheep and goat it is present only in the erythrocytes, while in the chicken it occurs both in the tissues and the erythrocytes. It is noteworthy that the chicken is a striking exception to the rule of non-infectivity. An attempt was made to increase the resistance of ducklings to *Plasmodium lophurae* infection by administering, at intervals of a few days subcutaneous injections of the hapten prepared from guinea-pig kidneys, horse kidneys and sheep erythrocytes. These were employed as fresh suspensions or extracts of various kinds, heated or unheated. In only one of the experiments, in which heated suspension of guinea-pig kidney was used did there appear to be any protection. It was not possible however to obtain a like result when the experiment was repeated. The conclusion is that attempts designed to increase the resistance of ducklings to the infection have yielded largely negative results. C. M. Wemyss

### BLACKWATER FEVER.

BRICKMAN G. & WERTHEIMER, E. Lysis of Red Blood Cells by Tissue Slices. *Brit J Exper Path* 1945 Aug v 28 No. 4 217-24. [11 refs.]

This is an account of an attempt to reproduce the findings of MACGRAITH *et al.* (this *Bulletin* 1943 v 40 584) in regard to lysis of red blood corpuscles in the presence of tissue slices. The authors confirm that washed tissue slices haemolyse washed red cells. They find that such lysis is inhibited by heat but not by serum, potassium cyanide or mercuric chloride and that pre-incubation of the tissues "shortens the induction period and results in more rapid lysis." The lytic power of tissue slices is not species-specific. The authors conclude that the lytic phenomenon depends on autolysis and stasis and is "not connected with normal or pathological blood destruction."

[PONDER (*J Gen Physiol* 1944 v 27 483) states that he had no difficulty in confirming the results of Macgrath *et al.* so far as the lytic effect of tissue slices was concerned. He found that the lytic agent was destroyed by heat, and by high and low pH. He agrees with the present authors that the lytic agent is not species-specific. Ponder considered that the tissue lytic agent was possibly similar to lyso-lectin. The present authors disagree with this. The disagreement that exists concerning properties of tissue lytic agents is probably due, fundamentally to the fact that there is, as yet, no well standardized biological technique for their investigation.] B. G. Macgrath.

## TRYPANOSOMIASIS

WEINMAN D & FRANZ K. Early Results of the Treatment of African Trypanosomiasis with Two New Arsenical Preparations (Melarsen Oxide and 70A) Preliminary Report *Amer J Trop Med* 1945 July v 25 No 4 343-4

Two new arsenicals were tested against sleeping sickness in Liberia —(i) Melarsen oxide (supplied by Parke Davis and Company) a trivalent arsenic oxide derived from the pentavalent Melarsen previously introduced into therapy by E. A. H. FRIEDLICH [literature references not cited by the authors see this *Bulletin* 1941 v 38 634 and *J Amer Chem Soc* 1944 v 66 1775] and (ii) a substance designated as 70A (supplied by Dr Harry EAGLE) the composition of which is undisclosed beyond the statement that it is a phenyl arsenoxide [Cf EAGLE *et al* this *Bulletin* 1945 v 42 15 EAGLE *ibid* 354]

(i) *Melarsen oxide*

Oral treatment 12 patients 8 of whom showed evidence of neurological involvement (5 with trypanosomes in the cerebrospinal fluid) were treated with 3 mgm. per kgm. daily for 5 to 8 days. The blood lymph glands and cerebrospinal fluids were clear of trypanosomes by the end of the course or in some late cases after a second course. The cerebrospinal fluid cell counts of the late cases fell after treatment in all instances though one of these patients was subsequently judged to have relapsed because four months after his second course the count was found to be higher than when examined the previous month.

Intravenous treatment 8 patients 3 with neurological involvement were treated by 0.1 mgm./kgm. daily for 7 days. Results in early cases were similar to those obtained by oral treatment. However 2 of the 3 late cases failed to respond. Nevertheless the authors write that for maximal effect the parenteral route is preferable to the oral [this is not borne out by the data which they present]

(ii) 70A

This compound was tried in 10 patients and the authors conclude that it was effective in the early stage but neither prevented nor ameliorated cerebral involvement. [It seems rather odd to credit a compound with effectiveness against the early stage of a disease whilst also charging it with inability to stem the progress of that disease.]

[The observation periods after treatment by Melarsen oxide apparently varied from 2 to about 4 months and this is quite insufficient for proper substantiation of the authors' claim as to the indisputable efficacy of Melarsen oxide in meningo-encephalitic cases. Their criteria of efficacy in cases of neurological involvement are inadequate as for example in the significance which they attach to the fact that in eight such cases the cerebrospinal fluid cell counts initially ranging from 65 to over 1,200 with an average of 357 cells per cmm declined after treatment to a range of 7-556 with an average of 138. To give point to this criticism the reviewer has applied Weinman and Franz's method of evaluating cerebrospinal fluid cell count changes to the data provided by HARDING in Table I (p 107) of his paper on the effects of antypol trypanamide and diamidines [this *Bulletin* 1946 v 43 103]. In seven cases treated by pentamidine or propamidine in which the initial cell counts were as in Weinman and Franz's late cases above 65 per cmm the counts in all individual cases were, as in Weinman and Franz's experience, reduced after treatment (4 to 6 months later) and the range of 74-536 with an average of 255 fell to a range of 3-17 with an average of 10 cells per cmm]

According to Wemman and Franz therefore pentamidine or propamidine would be judged highly efficacious in meningo-encephalitic cases which in fact they are not.

With regard to 70A, it is disappointing to find in a highly respected scientific journal that space is allowed for a description of the unpromising results of therapeutic trials with a compound whose formula is not revealed.]

E M Lowrie

LEWILLON R. Le piégeage expérimental de *Glossina palpalis* à la Mission Médicale du Kwango. [Experimental Trapping of *Glossina palpalis* at the Kwango Medical Mission.] *Rev. Travaux Sci. Méd. Congo Belge* 1945 July No. 4 45-57 2 figs.

Tsetse flies breed so slowly that they can sometimes be almost exterminated by measures aimed at destroying the adult flies. The Harris trap was markedly successful against *Glossina pallidipes* in Zululand, but gave disappointing results elsewhere, especially against *G. palpalis*. Two traps devised by SWYNNERTON—one using a flat shaded screen as an attractant and the other containing an animal (bullock or pig) have had a limited success in Tanganyika and elsewhere.

An easily and cheaply constructed trap made entirely from indigenous materials, and resembling in outline a man, is described here. The lower part is similar to the "crinoline" trap and the insects enter this from beneath. They then fly upwards to the light and find themselves trapped inside a hollow gourd pierced with numerous small holes to let in the light—the gourd represents the head.

When carefully sited in a heavily infested fly belt this new mannequin trap caught many flies and subsequently reduced the density. It was much more successful than the Harris trap and as good or better than the Swynnerton models—it was also the easiest and cheapest to construct.

As an anti-sleeping-sickness measure, trapping is compared with prophylactic injections of Antirypol (four injections per annum). It is more expensive to treat one individual than to construct four traps. The author considers that trapping is often the more practical measure.

Kenneth Mellanby

MAZZA, S. MIYARA, S. & JORG M E. Investigaciones sobre enfermedad de Chagas. Naturaleza de la reacción conjuntival en primer período de la enfermedad de Chagas. Enfermos comprobados exclusivamente por demostración de leishmanias de *S. cruzi* en biopsias conjuntivales. [Studies on Chagas's Disease. The Conjunctival Reaction in the Early Period. Leishmanial Forms of *T. cruzi* in the Conjunctiva.] *Universidad Buenos Aires. Misión de Estudios de Patología Regional Argentina (Ujujuy)*. Publicación No 69 1945 152 pp. 163 figs.

In an article published in 1944 the authors gave an account of the histopathology of the conjunctiva in the early stage of Chagas's disease [this *Bulletin* 1945 v 42, 792]. The present work is a sequel and an amplification of the former. The authors start by describing the projection microscope they use for examining biopsy specimens of the conjunctiva—the Zeiss Ultraphot and refer to the Fuchs Orthophot and the Ernst Busch Citophot. It is an adaptation of the trichinoscope to a microscope. The apparatus is depicted and the optical projection presented diagrammatically.

They then pass on to give very detailed descriptions of the histological changes in portions of the conjunctiva taken by biopsy from 20 patients. The ages of the patients varied from 5 to 63 years. In 8 of these the diagnosis

was in no doubt in 7 trypanosomes were found in the blood and in the other xenodiagnosis was positive in 5 others the Guerrero-Machado test was positive but not the blood examination nor xenodiagnosis in the remaining 7 none of these was positive and the diagnosis rested on the clinical history the general appearance and the histology of the sections made from the biopsy specimens

With a view apparently of driving home their point the authors indulge in a good deal of repetition. A record of the details of one case may be reproduced here to acquaint the reader with the histological changes present

From a man of 43 years on the sixth day after he had been bitten on the right eyelid by an infective bug a fragment of the conjunctiva was taken for section and examination. The changes are thus described. Marked alteration in the conjunctival structure due in part to inflammatory infiltration and in part to epithelial erosion. There is intense coagulation with haemorrhages some localized others more diffuse and serofibrinous oedema. There is moderate perithelial infiltration with small dense collars of perivascular infiltration constituting in places nodular masses with fibroblastic proliferation and oedema. There is no leucocytic invasion but atrophy with erosion and ulceration and the vessels are intensely congested to form a sort of telangiectatic granuloma. In the parts less acutely affected the nodules are smaller but the same epithelial atrophy is seen. Cytologically the usual types of cell associated with inflammatory processes are present together with proliferation of histiocytes and some fibroblasts mingled with myeloid infiltration and serofibrinous exudation. Among hyperplastic histiocytes there is a dense fibrin reticulum and thin connective tissue fibrils of the inflammatory new growth type. Certain parts showing the nodule formation show also multinucleate structures tending to a coagulative necrobiosis of the central connective tissue in the interior of which are free leishmanial forms of *T. cruzi*. Leishmania are commonly present in the macrophages and a few were seen in the walls of the capillaries. (The whole work is embellished with photographs of the patients depicting the palpebral oedema and with photomicrographs of the tissue changes beautifully reproduced.)

H. Harold Scott

## LEISHMANIASIS

DA CUNHA, A. M. Infecções experimentais na Leishmaniose tegumentar americana. [Experimental Mucocutaneous Leishmaniasis] *Mem Inst Oswaldo Cruz* 1944 Oct v 41 No 2 263-82 26 figs on 7 pls. English summary

Working with recently isolated cultures of *Leishmania brasiliensis* the author inoculated rhesus monkeys intradermally over the superciliary arches or on the nose. The course of the infection varied according to the type of lesion produced. Usually only a local lesion developed, in one to two months which healed in three to eight months. In some cases however involvement of the nasal mucosa occurred. When this happened it was not the result of direct extension from a cutaneous lesion which may occur as has previously been reported, but was due to the spread of the infection to the mucosa by some other channel. The nasal lesions which were in the form of nodules on the nasal septum and polypi which completely shut off the naso-pharynx showed no tendency to spread to the pharyngeal region. Though the cutaneous lesions healed those of the nasal mucosa persisted. Dogs were also successfully inoculated in the skin of the nose. One agouti (*Dasyprocta agouti*) and

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Kenneth McIlwain

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a monkey which had recovered from a previous infection were inoculated without result. The author points out that the development of extensive nasal lesions in the monkey affords further proof of the individuality of *Leishmania brasiliensis*

C M Wenyon

## FEVERS OF THE TYPHUS GROUP

VARLEY Florence M & WEDDON F R. Application of a Quantitative Complement Fixation Test to the Serum Diagnosis of Typhus Fever. *J Immunology* 1945 Sept v 51 No 3 139-46 [14 refs.]

The authors describe the highly specialized technique employed in a new quantitative method of carrying out the complement fixation test in the diagnosis of typhus fever. The method was devised by WADSWORTH, MALTNER and MALTNER in 1938 and is described by Wadsworth in his book *Standard Methods of the Division of Laboratories and Research of the New York State Department of Health*, 1939 Williams and Wilkins Co. Baltimore.

In the method the end point adopted is described as follows: 50 per cent. haemolysis of the cells present as a standard of reference rather than the point of complete haemolysis. This renders evaluation of the results much more precise and satisfactory. A set of four charts for use in carrying out the test is reproduced. Preliminary trials are said to show that lytic or slightly anticomplementary properties of the normal serum used for diluting the anti-serum under test do not influence the quantitative estimation of the amount of complement rendered inactive by the antigen-antibody mixture.

The new technique is not likely to appeal to workers other than those who have exceptionally complete laboratory facilities at their disposal.

John W D Megey

CIUCA, M. MESROBEANU L. BADENSKI, A. MUNTEANU G & PARACHEVESCU N. L'antigène glucido-lipidique des Proteus X est le facteur responsable de la réaction Weil-Felix. [The Gluco-lipid Antigen of Proteus X is the Factor Responsible for the Weil-Felix Reaction.] Reprinted from *Rev. Spinaltor Med.* Bucharest 1941 Feb-Mar Nos 2/3, 7 pp.

CIUCA, M. MESROBEANU L. BADENSKI A. FRANKY M. & MUNTEANU G. Contributions à l'étude de la toxicité de l'endotoxine glucido-lipidique du Proteus X. [The Toxicity of the Gluco-lipid Endotoxin of Proteus X.] Reprinted from *Rev. Spinaltor Med.* Bucharest 1941 Feb-Mar Nos. 2/3 14 pp.

CIUCA M. & MESROBEANU L. II. Sur la structure antigénique des variantes du B proteus. Caractères physicochimiques de l'antigène glucido-lipidique du Proteus X19. [The Physical and Chemical Characters of the Gluco-lipid Antigen of Proteus X19.] Reprinted from *Bull. Sect. Sci. Acad. Roumaine* Bucharest 1941 v 23, No 7 310-20 [23 refs.]

SCHÄFER, H. H. Stoffwechseluntersuchungen an Fleckfieberkranken. [Investigations into the Chemical Changes in Typhus Patients.] *Deut. med. Woch.* 1944 July 21 v 70 Nos. 29/30 417-19 2 figs. [20 refs.]

The author has studied the chemical composition of the blood and urine of several patients during severe attacks of typhus fever.

The pronounced fall in the chloride content of the urine during the acute stage of the fever was not accompanied by any evidence of chloride retention.

in the blood there was instead an appreciable diminution in six of the eight cases investigated. In five of these six cases the serum sodium range was 184-216 mgm. per cent and the chlorine range was 284-334 mgm. per cent. No pronounced fall was observed in the serum calcium which ranged between 8.2 and 10.0 mgm per cent. The potassium content of the serum was considerably increased especially in very severe attacks in which the findings ranged between 23.4 and 74.5 mgm per cent. The residual [non protein] The serum proteins were rather low in all the cases investigated during the second week they were 4.88-7.6 gm per cent. The residual [non protein] nitrogen was not greatly increased it was only 21 mgm. per cent in a fatal case and in the other four very severe cases it was 45-63 mgm per cent during the second week. The author concludes that great increases up to 100 mgm per cent or more occur only in cases complicated by glomerulonephritis which was common during some epidemics in extremely cold weather. The findings especially in connexion with the chlorides suggested changes in the permeability of the capillary walls associated with a diminution in the volume of the blood plasma and a resultant fall in the blood pressure. The condition is described as one of transmineralization. *John W D Megaw*

DUENSING F Über pathologische Fremdreflexe bei Fleckfieber Encephaliden von choreatisch-myoklonischem Gepräge [Unusual Pathological Reflexes of Choreiform-Myoclonic Type in the Encephalitis of Typhus Fever] *Der Nervenarzt* 1944 Mar-June v 17 Nos 36 73-80 [10 refs]

Two cases are described in detail in which the patients suffered from a choreiform myoclonic syndrome after attacks of typhus fever. The abnormal reflexes were of a type that the authors had never seen except in athetosis myoclonus and occasionally in Parkinsonism after encephalitis. The condition persisted for at least 14 months and though there was some improvement by the end of that time it seemed unlikely that complete recovery would ever happen. *John W D Megaw*

GÄRTNER W Erkrankung von Tonussteuerungszentren bei Fleckfieber [Affection of the Tonus-Controlling Centres in Typhus Fever] *Der Nervenarzt* 1944 Mar-June v 17 Nos 3/6 80-86

The author describes and discusses at length a peculiar case of mental disorder which began 17 days after defervescence from a severe attack of typhus fever. The symptoms were varied and at different times suggested schizophrenia hysteria and hypnosis.

The main drift of the author's argument is that the manifestations resulted from damage to the nerve centres of the mesencephalon which control various mental chemical and mechanical functions of the body. The patient was observed for four months and although he had made a complete physical recovery his mental condition was still far from normal. The author stresses the need for an investigation by a psychiatrist in all cases in which a soldier commits offences against discipline after having suffered from typhus fever. *John W D Megaw*

RAETIG H Die fraktionierte Rekonvaleszenzserumbehandlung des Fleckfiebers [The Treatment of Typhus Fever with Fractional Doses of Convalescent Serum.] *Med Ztschr* 1944 Nov v 1 No 2 59-60

Having had unsatisfactory results from single large doses of convalescent serum the author decided to try small doses given daily by the intravenous

route. The treatment was started as early as possible and was continued till defervescence. At first the doses were 20-40 cc. but later they were increased to 40-60 cc. and better results were obtained with the larger doses especially in severe attacks.

In a large number of cases treated in this way the case fatality rate was 7.5 per cent as compared with a rate of 18.3 per cent among control patients. Although alternate controls were not employed the author insists that patients in whom the onset was specially severe were selected for the treatment and that the number treated (more than 300) was so large that the element of chance was eliminated.

John W D Meyer

LE GAC P Un cas mortel de typhus tropical constaté en Haute-Côte-d'Ivoire.  
[A Fatal Case of Tropical Typhus in the Upper Ivory Coast.] *Méd Trop*  
Marseille. 1942 June v 2 No. 6 473-7

The clinical features of a sporadic case of typhus-like fever are described the patient died on the 12th day.

The Weil-Felix reaction was tested on the 10th day. *Proteus* O1A was feebly agglutinated at a titre of 1-50 the O1B and O1C strains were not agglutinated. A Patas monkey and two rabbits were inoculated with the patient's blood, each animal received 5 cc by the intraperitoneal, and 1.0 cc. by the intraocular route. Indocyclitis was caused in the monkey and in one rabbit which also had a febrile reaction, but injections of its brain substance caused no reaction in a monkey two rabbits and two white rats. In the Weil-Felix responses in the originally inoculated animals, the highest titres were 1-60 in one rabbit against O1B and 1-100 in the monkey against O1A.

The author regarded boutonneuse and tick fever as being excluded because the patient had neither the very characteristic massive eruption nor the O1C reaction observed in these fevers. He concluded that the disease was "related to Malayan typhus or the jungle typhus of Bengal."

[The evidence in support of a diagnosis of mite-borne typhus and against that of tick borne typhus does not appear to be convincing but judgment can be reserved because the author states that 15 other cases from different parts of the Upper Ivory Coast are being studied.]

John W D Meyer

TORRINGTON H. Tsutsugamushi Disease (Scrub Typhus). The Effects of an Immune Rabbit Serum in Experimentally Infected Mice. *Pub Health Rep* Wash. 1945 Oct 12 v 60 No. 41 1215-20

Serum of rabbits immunized by rickettsiae of tsutsugamushi disease was found capable of preventing the death of mice infected by lethal doses of homologous strains of rickettsiae. The serum was injected subcutaneously and was effective in some cases, even when given up to 72-168 hours after the time of infection. Serum of one of the four rabbits used was relatively ineffective. Large doses were more effective than small.

The rabbits were immunized by intravenous injections of infected yolk-sac material given on two consecutive days weekly for three weeks, and the serum was collected 19 days after the last injection.

The antibody content of the serum was increased by a further series of injections given after a resting period of several weeks.

Tsutsugamushi disease is regarded as specially favourable for serum treatment because of the possibility of immediate diagnosis at the time of onset in many cases owing to the presence of the eschar.

The author mentions that he has already found penicillin ineffective in the treatment of infected white mice and that ANDREWS, KING and VAN DEN

ENDE have had similar negative results with para sulphonamido-benzamidoime hydrochloride. [For the results of this drug in experimental typhus see this *Bulletin* 1945 v 42 20] *John W D Megaw*

FINNEGAN Susan *Acarid as Agents transmitting Typhus in India, Australasia and the Far East*

This book is reviewed on p 262.

## YELLOW FEVER.

DÍAZ I *Brote de fiebre amarilla selvática en Venezuela durante el año 1944* [Outbreak of Jungle Yellow Fever in a Venezuelan Area in 1944] *Boletín Oficina Sanitaria Panamericana* 1945 July v 24 No 7 589-96 1 map English summary

An outbreak of jungle yellow fever occurred in an area close to the Andean range in the States of Barinas, Bolívar and Táchira in Western Venezuela, near the Colombian border. First suspicions of the presence of the disease were aroused by the examination of a viscerotomy specimen from a patient from Cuíte who died on July 22 at the Hospital Vargas of the city of San Cristóbal in the State of Barinas. It was also found out that in the section of San Cristóbal-La Colorada highway several fatal febrile cases with blood vomiting had occurred about the same time. The chief of the Yellow Fever Division of the National Department of Health proceeded on September 3, 1944 to the area in question with a laboratory worker and an entomologist. A total of 12 cases of yellow fever, all of the jungle type, were verified by viscerotomy in areas completely separated in the three States involved. Two of the cases were in the State of Barinas, located in an oil camp in a jungle zone between the Andean range and the Barinas plain. In the State of Táchira nine fatal cases were verified and 21 other cases were studied clinically and epidemiologically, which were confirmed as yellow fever by the mouse protection test performed in the surviving patients. In the State of Bolívar so far considered the only endemic yellow fever zone in Venezuela, only one case was found in a jungle area near San Félix on the Orinoco river. It is supposed that in the whole area affected there must have been about 120 cases with a 70 per cent death rate. (The last two patients reported were from La Tigra, about 16 miles S.W. of Barinas and died in the Barinas hospital on November 29 and December 6 respectively.) Precautionary measures were immediately taken through the local Health Authorities including a campaign against *Aedes aegypti* in urban districts, temperature-taking of all travelers, checking by the health authorities of febrile cases admitted to hospitals and general vaccination against yellow fever. By the end of the year 28,263 vaccinations had been made as follows: State of Apure 3,162; Barinas 5,000; Táchira, 17,342; Zulia 1,357; Bolívar 1,402. In the State of Bolívar 14,000 persons had already been vaccinated during the two previous years. This represents about 50 per cent of the total population and leaves unprotected only the Indians deep in the jungle.

POLAK Marius Frans *Vraagstukken der gele koorts. Epidemiologie en vaccinatie*

This book is reviewed on p 264.

WADDELL, Mary B. Persistence of Yellow Fever Virus in Mosquitoes after Death of the Insect. *Amer J Trop Med* 1943 July v 25 No 4, 329-32.

*Aedes aegypti* were fed on marmosets or Cebus monkeys infected with jungle strains of yellow fever and subsequently tested for virus content by intra cerebral inoculation into white mice.

The mosquitoes were then killed either by chloroform, ether potassium cyanide or tobacco smoke and after varying time intervals groups of five were tested for virus content.

It was found that after death of the mosquito from chloroform, most of the virus activity was lost in 30 minutes and was completely absent after 1 hour. On the other hand significant amounts of yellow fever virus were recovered from the bodies of mosquitoes killed by the other three methods two hours after being killed, and were still present up to 45½ hours in those killed by potassium cyanide. Virus was also recovered from *Aedes aegypti* that had died of starvation up to 25 to 41 hours after death.

Specimens of *Haemagogus equinus* and *H. spegazzini* which had died spontaneously after feeding on infected monkeys, were collected at intervals of from 1 to 3 days and tested for the presence of virus. It was recovered from mosquitoes collected within 24-48 and 72 hours after death, the exact time of death being unknown.

The use of ether is recommended as the most satisfactory method of killing insects when it is intended to use them in attempts to isolate yellow fever virus.

E. Hindle

See also p 255 HADDON A J The Mosquitoes of Bwamba County Uganda.

SMITHBURN K. C. Experimental Studies on the Yellow Fever Protection Test. *J Immunology* 1945 Sept. v 51 No 3 173-89 [10 refs.]

In 1930 THEILER [this Bulletin 1930 v 27 872] discovered that white mice were susceptible to yellow fever virus. This led to the development of the intracerebral neutralization test of Theiler (*ibid* 1933 v 30 714) and to the intraperitoneal test of SAWYER and LLOYD (*ibid* 1932, v 29 198). The latter was the simplest method for estimating protective antibodies in human and animal sera, and was used on a large scale in epidemiological studies and in the evaluation of immunity produced by various vaccines. More recently, WHITMAN in Brazil with the intraperitoneal test (*ibid* 1943 v 40 534) and BUGNER in Colombia with the intracerebral test (*ibid* 1941 v 38 434) have devised modifications which have advantages over the standard intraperitoneal test.

For various reasons these tests proved unsatisfactory under the conditions present in Uganda, and it became necessary to find some satisfactory modification.

It is known that immature white Swiss mice are much more susceptible to the virus than older ones, the decline in susceptibility being rapid in the first three weeks of life but after that time slow. Infant mice are highly susceptible to intraperitoneal inoculation. This susceptibility decreases rapidly in the older mice, but can be enhanced 10- to 15-fold by a preparatory intracerebral injection of starch solution. The use of younger mice also means that less serum can be used than is necessary in standard tests with 6-week-old mice.

Smithburn found that not only were 7-day-old mice more susceptible than older mice to the virus, but also that antibody protects against more units of effective virus in them. Similarly in 14-day-old mice the titre of antibody in

a known immune serum was twice as high against 10 times the number of effective units of virus as it was in 35-day-old mice. This suggested that smaller amounts of antibody would be detected if weaker virus was used in the immature mice.

It was found that a serum which gives an inconclusive result against a relatively strong dilution of virus will give fully protective results if the balance between virus and serum is not too heavily weighted by the former.

In sera which had previously given inconclusive results with the standard 10 per cent virus test tests with 1 per cent. virus indicated that an occasional serum which originally gave a protection ratio of 0/6 may be protective that if one mouse survived originally there is an even chance that the serum is protective and that if more than one mouse survived it is almost certainly protective.

The final test decided on in Uganda uses 1 per cent. virus instead of 10 per cent as used by Sawyer and Whitman. If 3.0 ml or more of serum are available the tests are done in groups of six mice 5-6 weeks old. They receive an intracerebral inoculation of 2 per cent. starch solution and almost immediately afterwards receive intraperitoneally 0.6 ml of a mixture of 3.0 ml serum and 1.5 ml of 1 per cent virus. The mixture is not incubated prior to inoculation. If less than 3.0 ml serum are used the test is done in groups of 8-10 fourteen day-old mice comprising two litters. They do not receive starch inoculation. Each mouse receives 0.06 ml intraperitoneally of a mixture of 0.5 ml of serum and 0.25 ml. of 1 per cent virus. The results of these tests are interpreted as follows. If not more than 1 mouse dies the serum is considered protective. If not more than 2 mice survive the serum is regarded as non protective. If more than 1 mouse in a group die and more than two survive the result is regarded as inconclusive. Re tests are made on such sera whenever enough is available.

F O MacCallum

BUGHER J C. The Effect of Prolonged Storage of Sera on Yellow Fever Protection Tests. *Amer J Trop Med* 1945 July v 25 No 4 333-8 2 figs [11 refs]

Yellow fever immune sera that had been stored in glass ampoules at Yaba Nigeria under very unfavourable conditions for more than 12 years were tested by means of the intraperitoneal protection test. Although the average loss of protective power seems to be about 50 per cent each year there were considerable individual differences and some of the sera still contained demonstrable antibodies. On the other hand in some instances the deterioration may be greatly accelerated. The velocity of deterioration seems to resemble that recorded by GLENNY in the case of diphtheria antitoxin [see *J Hygiene* (Camb) 1913 v 13 63].

Previously negative sera stored under the same conditions gave uniformly negative results [See also this *Bulletin* 1945 v 42 800] E Hindle.

## DENGUE AND SANDFLY FEVER.

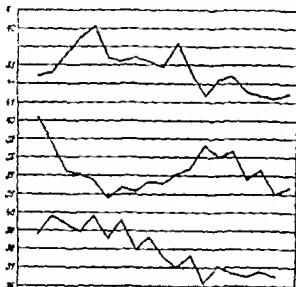
GOLDECK H & WALTHER R. Zur Frage des Russischen Kopfschmerzfiebers. [An Enquiry Into Russian Headache Fever] *Klin Woch* 1944 Feb 19 v 23 Nos. 5/8 59-61 3 figs.

This paper contains additional information regarding the problem fever Russian headache fever which is stated to have been common on the

eastern front during the recent war. No reference is made to the original description of the disease by SCHULZEN and BROGLIE [see this *Bulletin* 1944 v 41 127].

The author mentions the occurrence of 8 severe and 12 mild cases of the disease among 38 Russians in one camp. He saw about 50 cases but deals specially with 10 severe "meningeal" attacks in which stiffness of the neck was a prominent feature. The duration of the fever was 3-5 days in six, 7 days in two, and 8-10 days in two.

The cerebrospinal fluid was sterile on culture. It contained a considerable amount of albumin and numerous white cells, mostly lymphocytes; the cell count ranged from 37 to 1,070 per cmm. It is stated that even in the mild cases the white cells were increased, the counts ranging from 10 to 100. The headache is described as being localized in the occipital region. There was pronounced bradycardia.



Temperature Curves in Russian Headache Fever  
[Reproduced from *Klinische Wochenschrift*]

The three fever curves illustrating the paper show a striking resemblance to types commonly seen in dengue or sandfly fever, and the author states that the curve was of the saddle-back type in more than half the cases.

No information is given with regard to epidemiological conditions connected with the occurrence of the disease, even the seasonal distribution of the cases is not mentioned.

John W. D. Mearns

## PLAGUE.

COMTE, L., POURSIDES Y. & MOUSTARDIER G. La peste expérimentale du cobaye et du rat blanc (données anatomo-cliniques) [Morbidity Anatomy and Histology of Plague in the Guinea-pig and Rat.] *Méd Trop* Mar seilles. 1944 Mar-Apr v 4 No 2, 111-29, 10 figs on 4 pls.

Five guinea-pigs and six rats were used and were inoculated intraperitoneally, subcutaneously and subconjunctivally with suspensions of 48-hour aseptated

cultures A number of photographs of the histological lesions in liver lungs suprarenals heart and kidney accompany the text. Three grades of acute lesions are distinguished Necrosis and parenchymatous degenerations constitute the chief histological features in each organ and are recognizable in two types as toxic and septicæmic with abscess formation *W F Harvey*

MATHUR W & GOYAL R. The Treatment of Plague with Sulphathiazole. *Indian Med Ga* 1945 Aug v 80 No 8 383-5

Sulphathiazole has now become standard treatment in plague It was used by the authors in 81 out of 120 patients along with some adjuvant treatment such as a tablet of nicotinic acid 15 minutes previous to each dose if nausea was pronounced or 10 per cent soluseptasine and 15 cc of 25 per cent glucose parenterally to combat toxæmia Digitalis or coramine were additions if cardiac weakness set in There were 17 deaths in all *W F Harvey*

### CHOLERA

SEAL S C The Problem of Endemicity of Cholera in Bengal. (A Plea for further Investigation.) *Indian Med Gaz.* 1945 Aug v 80 No 8 414-17 [10 refs.]

The author has himself taken part in the important researches on the epidemicity and endemicity of cholera which have been conducted in India for very many years Answers were or are still required to the questions (1) What is a true cholera vibrio? (2) What is the best method of its recognition? and (3) What is its relation to other types of vibrio found in human beings water etc.? The Bengal Cholera Field Enquiry found that *V cholerae* could not be isolated from the stools of the general population or from water in the endemic area except in direct relation to the cholera case. Cholera is in fact transmitted from case to case and close contact carriers or water are only allowed infective agency for short periods and at short range It is interesting to note that an area is classed as "endemic" if during the last 32 years there were not more than 30 months in which cholera deaths were not recorded and if the maximum period of absence of cholera records was less than 5 months. Many questions are presented for solution and for the most part the conclusion is reached that a final verdict is still awaited The problem of primary importance in the epidemiology of cholera is the mystery involved in its endemicity In question form this is put as Where and how does the cholera vibrio exist before a case occurs in the endemic area?

*W F Harvey*

BINSON G Etude des principaux caractères de 94 souches de vibrions et de quelques épreuves utilisées dans le diagnostic bactériologique du choléra. (Note préliminaire.) [Vibrio Characters and Tests for Cholera.] *Méd Trop* Marseilles 1944 Jan.-Feb v 4 No 1 32-48 [29 refs.]

A collection of 94 laboratory strains of vibrio were at the disposal of the author and have been tested diagnostically They are classified as (1) isolated from cholera cases (2) of indeterminate origin (3) water vibrios and (4) El Tor vibrios (true and Macassar strains) This is a preliminary note and takes up specially—I Biochemical reactions (a) sugar fermentation and the classification of HEIBERG (b) the cholera red reaction (c) the Voges-Proskauer test II Haemolysis III OH agglutination and the thermostability test of



**GIPSEN** These are for the most part standard tests. Some of the conclusions may be recorded briefly in serial order —I Heiberg's Group I is constituted essentially by agglutinable organisms from cases of infection with the true cholera vibrio. The cholera-red reaction is not a singular characteristic of the true cholera vibrio. A rather high probability value attaches to the Voges-Proskauer test in differentiating between the true cholera vibrio and the original El Tor but an exception has to be made for the Celebes strain of Macassar. II Haemolysis as a standard is much disputed, but affords a striking differential character with sheep erythrocytes capable of separating the non-haemolytic cholera vibrio from the haemolytic El Tor. III Agglutination does not separate the haemolytic vibrios especially the El Tor group from the non-haemolytic. The author lays very great stress on the Gipsen test because it is easy to carry out easy to read and economical of time which are very important considerations for the quarantine or frontier officer. This test is carried out as follows —An 18-hour agar culture is made into a dense suspension in a normal salt solution. One-half of this suspension is heated at 56–57°C for 3 hours and, when cool a comparison is made of the agglutinability of heated and non-heated suspensions kept at 46°C for 16 to 18 hours. Agglutination is read as being (a) with complete clearing, (b) with partial clearing or (c) with no clearing of the suspension. El Tor vibrios are completely thermotable and still show complete clarification, whereas vibrios isolated from cholera cases are thermolabile, that is, clarify only partially or not at all. The test should be a boon to the epidemiologist who has to apply detention measures to wayfarers with discernment.

W F Harvey

**PANJA G** An Easy Method of producing Permanent Rough Variation in Cholera Vibrios. *Indian Med Gaz.* 1945 July v 80 No 7 342-3

Rough colonies of Inaba and Ogawa subtypes of cholera vibrios were obtained by growing the smooth vibrios on a nutrient agar plate containing atabrin (Bayer) in a strength of 1:5000. Rough colonies appeared after a few days and were replated on ordinary nutrient agar. Both variants appeared to be permanent.

J F Corson.

**PANJA, G & GHOSH S K.** Viability of Dysentery, Enteric and Cholera Organisms in Milk Curd (*Dahi*). *Indian Med Gaz.* 1945 Aug v 80 No 8 390-92

Curdled milk or *dahi* is a universal food throughout India and it may be sweet or sour. Both types contain lactic acid bacilli and have a pH ranging from 4.2 to 4.7. The efficacy of these bacilli or their acid product is widely appreciated. As a test 4 drops of culture of dysentery, enteric and cholera organisms were severally added to about 10 cc. of dahi, and subcultures were made at fixed intervals. Cholera vibrios were killed within 5 minutes, typhoid bacilli in times varying from 5 minutes up to a maximum of one hour while dysentery organisms required from 30 minutes up to 4 hours. An interesting comparison is made between lactic acid and other acids such as hydrochloric, acetic and citric with adjustment in all cases to pH 4.4. It was found that these other acids had a poor bactericidal effect by comparison with lactic acid on dysentery and typhoid organisms and that all of them except citric acid were highly and quickly bactericidal to the cholera vibrio. Tests with lime juice showed that at pH 4.4 and in dilution it kills cholera vibrios in half an hour and undiluted (pH 2.8) in 5 minutes, but has no effect on *Bact. flexneri* or *Bact. typhosum*.

W F Harvey

## BACILLARY DYSENTERY

BOSE A N SEN GUPTA P N & BASU U P Sulpha Drugs in Bacillary Dysentery *Indian Med Gaz.* 1945 Aug v 80 No 8. 385-8 [19 refs.]

It is generally accepted that the sulphonamide drugs more particularly sulphaguanidine sulphapyridine succinyl sulphathiazole phthalyl sulpha thiazole and sulphanilyl benzamide and even sulphanilamide itself are more or less therapeutically beneficial in cases of bacillary dysentery. Sulphaguanidine is widely used, but it is costly and the dosage necessary is considerable its employment may be precluded by vomiting in those cases in most urgent need of it as it cannot be injected. Furthermore it is comparatively ineffective in *Bact dysenteriae* (Sonne) infections. Sulphapyridine is effective but causes nausea and vomiting and, possibly serious renal disorders if used in a dehydrating disease such as dysentery. Succinyl sulphathiazole is good, but again is inert against Sonne dysentery \* while phthalyl sulphathiazole is of low toxicity and is highly effective against Flexner infections. The activity of these acyl sulpha thiazole drugs is dependent in part on their breaking down to sulphathiazole or at least to some compound containing a diazotizable amino grouping in the system.

Sulphathiazole was found, by the authors the best bacteriostatic agent of the series against a variety of dysentery organisms in culture. sulphapyridine and sulphanilyl benzamide were found to approximate in activity to it while phthalyl sulphathiazole was inferior to these but superior to sulphaguanidine. Succinyl sulphathiazole and sulphanilamide proved the least effective of these compounds when examined *in vitro*.

Sulphathiazole is relatively inactive against bacillary dysentery when given by the mouth as it is readily absorbed from the gut. Succinyl and phthalyl sulphathiazole prepared by acylating the *p*-amino grouping of sulphathiazole are less soluble less readily absorbed and more therapeutically effective.

Sulphanilyl benzamide although it is readily absorbed, has proved even less toxic but equally effective in the treatment of bacillary dysentery (including Sonne infections) in the hands of the authors who therefore conclude that the activity of a sulphonamide in intestinal infections cannot be judged solely as an inverse measure of the degree to which it is absorbed from the gut.

Inquiries are proceeding to find out the factors on which the action of these drugs against intestinal infections depends. They think that sulphanilyl benzamide may be the drug of choice in the treatment of bacillary dysentery.

A R D Adams

PANJA, G The Action of Drugs on Dysentery Bacteriophage. *Indian Med Gaz.* 1945 June v 80 No 6 294-5

Experiments were made to see whether drugs used for the treatment of bacillary dysentery interfere with the action of dysentery bacteriophage. The drugs tested were sulphapyridine sulphaguanidine solusoptasme phenol and electrolytic chlorine. The bacteriophage was used both concentrated and much diluted, and the drugs were used in two strengths the sulphonamide in 1 and 2 per cent solutions and suspensions phenol in 0.5 and 1 per cent solution and chlorine in 0.25 and 0.5 per cent solution. The drugs were kept in contact with equal quantities of the phage at room temperature for one or two hours then filtered through  $L_2$  candles the filtrates were tested for the presence of phage by their effect on cultures of dysentery bacilli on a solid medium. The details are shown in tables.

In addition to the experiments with drugs dysentery phage was boiled for 2 and 5 minutes and tested similarly for activity.

The author concluded that these drugs have no action on strong dysentery phage and that boiling a strong phage for 5 minutes does not completely kill it.

[March, 1946]

J F Corson

# AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

ENGLISH, R. B. Carriers of *Entamoeba histolytica* in Africans of Northern Rhodesia. *South African Med J* 1945 Oct. 27 v 18 No. 20 380

In the Northern Rhodesian copper-mining town of Luanshya, with a population of 2,500 Europeans and 30,000 Africans dysentery is almost exclusively of the bacillary type acute amoebic dysentery with trophozoites of *Entamoeba histolytica* being very rarely met with. Chronic amoebiasis in Europeans however appears to be becoming more common and causes anorexia, lassitude and inability to concentrate. Cysts are present in the faeces and the symptoms disappear with appropriate treatment. Because of this apparent increase among Europeans the author decided to determine the carrier rate among the African employees of the Roan Antelope copper mine.

Fresh preparations of faeces in saline and in Donaldson's eosin iodine mixture were examined microscopically. Cysts of *E. histolytica* were found in 170 (33.4 per cent) of the 509 Africans examined. Only 11 were minute forms.

The author mentions as interesting features of the local strain or strains of *E. histolytica* that (1) few cases of true amoebic dysentery occur (2) hepatic or other amoebic abscesses rarely occur (3) trophozoites of *E. histolytica* are rarely seen in Africans even in the frequent stools passed when they are suffering from bacillary dysentery. The local forms of *E. histolytica* appear to have low virulence but since Africans are employed as domestic servants and handle food in European households, the high carrier rate among them represents a very definite public health problem.

ATZEL, J. C. Incidence of Amoebic Carriers in Bombay. *Indian Physician* 1945 Nov. 4 No. 11 244-9 [23 refs.]

Out of 125 apparently healthy persons between the ages of 16 and 39 years, one faeces examination showed some protozoal and parasitic infection in 87 (33.6 per cent). 54 (43.3 per cent) had *Entamoeba histolytica*. In all these 54 cases the trophozoite stage was noted though cysts were present in some. The presence of *E. coli* and other protozoa was not particularly sought for but the former was detected in six along with *E. histolytica* and in four without. *Giardia intestinalis* was recorded three times and *Trichomonas hominis* once only. In nine cases ova of parasitic worms were found. The evidence available shows that, even though *E. histolytica* carriers as in this series are free from symptoms and are apparently healthy they should be regarded as clinically infected and consequently should be treated.

[The high percentage of trophozoites of *E. histolytica* in so-called carriers is against the testimony of experience of most workers, and certainly deserves further investigation.]

P. Manson-Baker

PATEL J C Incidence of Chronic Amoebiasis in Bombay and Non-Dysenteric Amoebic Abdominal Syndromes. *Indian Physician* 1945 Nov v 4 No 11 249-55

During 1944 101 stools of persons attending the Out Patient Department of the Singhanee Hospital Bombay were examined. These patients were suffering from symptoms related to the gastrointestinal tract. The presence of *E. histolytica* was particularly sought for other non pathogenic protozoa were not recorded. The dysentery amoeba was found in 58 in trophozoite form in 44 and in the cystic stage in 30 in 14 cysts alone were present. Of those with positive stools the youngest was six months old the oldest 55 years. The symptoms which varied in duration from a few days to 7 years were as follows —

Pain in the abdomen or diarrhoea vague pain most in the epigastrium or in the right or left iliac fossa flatulence and abdominal discomfort vomiting and hiccough low fever lassitude headache and giddiness lack of appetite stomatitis pain in the chest and back apathy and listlessness. In the case of females irregular catamenia and excessive leucorrhoea loss of weight

It is emphasized that chronic amoebiasis is more prevalent than is generally imagined and is responsible for chronic ill-health

[This paper represents the popular and widely-held attitude to amoebiasis and rests on a rather uncritical appreciation of symptoms which are common to a large section of the community in whom no evidence of protozoal infection can be obtained.]

P Manson Bahr

BIENKRANT W B GREENBERG M & MOST H Amoebiasis in a Hospital for the Insane. *Amer J Pub Health* 1945 Aug v 35 No 8 805-14 1 chart [13 refs.]

In an investigation carried out in a hospital for the insane by the New York City Department of Health over a period of 15 months 95 cases of amoebic dysentery were discovered among 5 575 inmates and employees. In mild cases diarrhoea was the chief and often the only symptom blood being absent from the stools and there being no fever. In severe cases diarrhoea was marked and the stools were frequent and in all cases blood was present many patients experienced abdominal cramps and all had fever. Examination of 1,822 persons showing no symptoms revealed 124 carriers of *E. histolytica*. Examinations were carried out on iodine and saline preparations of fresh warm specimens and on material concentrated by the zinc floatation method of Faust. In all 219 infections with *E. histolytica* were identified. Of these 61.5 per cent were found on the first examination, the second, third, fourth and fifth examinations bringing the percentages to 80.5 93 97.6 and 98.5 respectively.

Patients with amoebic dysentery were taken into hospital and treated in the following manner. A daily injection of emetine hydrochloride (0.06 gm.) for three days concurrently with chiniofon (12 tablets of 0.25 gm. each daily) for 10 days. After a 4-day rest period, carbarsone (one tablet of 0.25 gm. four times a day) was given for 10 days. In acute cases as distinct from carrier cases after a further rest period of four days a seven-day course of diodoquin was instituted (12 tablets of 0.2 gm. each daily). This completed what is described as intensive treatment on the 35th day. It is stated that clinical and laboratory cure was obtained in all cases. Presumably this refers to the immediate result for some months later there were 9 recurrences (or re-infections) 5 symptomless and 4 clinical cases. As regards infections among the inmates these were particularly high in those with poor sanitary habits. Of

[March 1946]

688 employees, 374 were inmate employees who gave an infection rate of 14 per cent. while the 314 paid employees gave a rate of only 8 per cent. It would seem inadvisable therefore to employ inmates in food-handling occupations. C. M. Wenyon.

KIRBY H. *Entamoeba coli* versus *Endamoeba coli*. J. Parasitology 1945 June v 31 No. 3 177-84 '33 refs.]

In this article the author has attempted to settle the controversy which has been waged for some years over the use of the two generic titles—*Entamoeba* and *Endamoeba*. He as others have done advocates the use of the former for the amoeba of the cockroach and the latter for the well-known parasites of man [this Bulletin 1945 v 42 327]. The following is his conclusion —  
Opinion 89 of the International Commission on Zoological Nomenclature does not constitute proof that *Entamoeba* Casagrandi & Barbagallo 1895 cannot be used as a generic name. Its argument rests on two points that *Entamoeba* is a homonym of *Entamoeba* and that *Blattella* is the type species of both, so that *Entamoeba* falls also as a synonym of *Entamoeba* Ledy 1879. The latter point which is the only one brought out in the summary of Opinion 89 is not acceptable. The Opinion asserts, but does not demonstrate that it is a homonym and there is nothing elsewhere in the Rules or Opinions that warrants the assertion. It is appropriate to place the species *coli* and *Blattella* in separate genera and it is considered that *Entamoeba* Casagrandi & Barbagallo 1895 is available as a generic name for *coli* and congenic species at the same time that *Endamoeba* Ledy 1879 is used for *Blattella* and congenic species " C. M. Wenyon.

SHIH LU CHANG. Studies on *Entamoeba histolytica*. V. On the Decrease in Infectivity and Pathogenicity for Kittens of *E. histolytica* during prolonged In Vitro Cultivation and Restoration of these Characters following Engraftment and Direct Animal Passage. J. Infect. Dis. 1945 Mar-Apr v 76 No. 2, 128-34 '31 refs.]

The author has studied two culture strains of *E. histolytica* from the point of view of their infectivity and pathogenicity to kittens. One strain lost its infectivity after 8 years of culture and remained non-infective for the following 3 years. The other strain became non-infective after 2½ years of culture. It was found that in both cases the loss of infectivity was associated with the cessation of encystation and that when encystation was again induced by transferring to encystation medium the infectivity was re-established. This infectivity which was evident after administration of material either orally or intra-caecally occurred only if the rectum was ligated. As plugging of the rectum was not sufficient it is concluded that the ligation did more than merely stop the passage of the intestinal contents. It appeared to alter the physiology of the intestine. When the infectivity of the first strain was re-established it was found that pathologically it was as active as it was originally. In the case of the second strain the pathogenicity was much reduced. It was regained to some extent by rapid passage from kitten to kitten. The bacteria associated with the pathogenic strain of *E. histolytica* were administered concurrently with the amoebae which had ceased to be infective. This failed to re-establish infectivity. When such a strain had regained its infectivity the administration of the virulent bacteria concurrently with the amoebae appeared to encourage the production of more severe lesions. C. M. Wenyon.

ZUCKERMAN Lucile K. & MELENEY H. E. A Fluid Medium for the Encystation of *Endamoeba histolytica* under reduced Atmospheric Pressure *J Parasitology* 1945 June v 31 No 3 155-7

To prepare the medium Cerophyl a commercial product made from the dried leaves of young cereal plants is extracted in CPR medium which consists of cholesterol one part per million and Difco proteose peptone 5 per cent. in Ringer's solution. The Cerophyl powder is added to the medium in a concentration of 2 per cent. The suspension is autoclaved and filtered and finally distributed in 50 cc. amounts in 250 cc. Erlenmeyer flasks. Just before inoculation with amoebae to each flask is added 5 cc. of inactivated horse serum and 0.02 gm. of specially prepared rice starch. After inoculation the flask is fitted with a rubber stopper and glass tube to enable the air pressure to be reduced to 40 mm. of mercury before incubation is commenced. It was found that without reduction of air pressure multiplication of amoebae prior to encystment was limited. By the use of this medium for over a year 100 flasks gave an average count of close on four million cysts per flask. C. M. Wenyon

MELENEY H. E. The Relationship of Clinical Amoebiasis to various Strains and Growth Requirements of *Endamoeba histolytica* *Puerto Rico J. Pub Health & Trop Med* 1944 Sept. v 20 No 1 59-70 [Refs. in footnotes] [Spanish version 71-83]

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

PAVLOVSKI E. N. & SKRUVINNIK A. N. [On the Period during which Females of *Ornithodoros papillipes* are able to transmit the Tick Relapsing Fever] *Zool Zh. Moscow* 1945 v 24 No 3 161-4 English summary [In Russian.] [Summary taken from *Rev. Applied Entom.* Ser. B 1945 Nov. v 33 Pt 11 165]

Of a batch of 24 nymphs and adults of *Ornithodoros tholozani* Lab. & Mègn. (*papillipes* Bur.) taken in October 1931 in a cave near Stalmabad (western Tadzhikistan) and brought to Leningrad 14 were alive in February 1933 ten in May 1934 six in April 1935 three (all females) in October 1940 and two in January 1941. During these years the ticks were allowed to feed at intervals on laboratory animals and they transmitted spirochaetes of relapsing fever with which they were naturally infected, to guinea-pigs and *Dryomys modestus*. In September 1941 the two surviving females were sent in a thermos flask to Samarkand, where they arrived in October 1942. They had not fed for about two years and one of them was dead in the following month. The other was taken back to Leningrad in June 1944 together with an adult male that had been found in western Kirghizia in 1935 and both were allowed to feed on a guinea-pig in October 1944. The latter subsequently showed spirochaetes in its blood and as the male had failed to infect laboratory animals on any of the occasions on which it had fed alone it is concluded that they were transmitted by the female.

Previous investigations by the authors have shown that *O. tholozani* can live for up to 25 years and can resist starvation for up to 7½ years. Its long life, the fact that spirochaetes persist in it from generation to generation its wide range of hosts other than man and domestic animals and its tendency to move about little ensure the preservation in nature of foci of relapsing fever.

WISSEMAN C. L. Jr. Relapsing Fever in Denton County Texas. Report on finding the Tick, *Ornithodoros tickhamsi* Naturally Infected. *Amer J Trop Med* 1945 July v 25 No 4 339-42, 2 figs. [10 refs.]

The author has succeeded in finding *Ornithodoros tickhamsi* infected with relapsing fever spirochaetes, in a cave near Roanoke Denton County Texas. It may be recalled that although this cave was suspected of being responsible for a number of human cases of relapsing fever [see this *Bulletin* 1935 v 32, 296] previous investigators had failed to find any infected ticks.

Three trips were made to the cave and each time ticks were collected from the sandy floor. Two members of the first party found ticks on their bodies, and seven days after being bitten one of them developed a typical attack of relapsing fever. Nine ticks were fed on a human patient undergoing pyretotherapy and after five days he showed spirochaetes in the blood and had 4 relapses at intervals of 3 to 5 days. Spirochaetes were present during each febrile attack.

White rats were readily infected by the inoculation of blood from both human cases. E. Hindle

JARVIS J. F. Relapsing Fever in an Infant of Five Days. *East African Med J* 1945 Sept. v 22, No 9 311

An African woman was admitted to Morogoro Hospital, Tanganyika Territory on April 8th 1945 developed relapsing fever on April 13th and gave birth to a child a few hours afterwards. Spirochaetes were present in her blood. The child remained apparently well until the 5th day when it also developed relapsing fever and died next day in spite of having received a dose of 0.015 gm. of neosarsphenamine (N.A.B.).

The author thinks that the mother might have been infected in February as she gave a history of having had fever about that time or she might have been bitten by a stray tick while in the hospital between April 8th and 13th. He suggests that the child might have been infected from the mother through the placenta, or by entry of the maternal blood into an abrasion or the cut cord (could infection by a stray tick be excluded?). J. F. Corson.

CHARTERS A. D. Louse-borne Disease. Correspondence.] *East African Med J* 1945, Sept. v 22, No 9 303-9

WOHMAN this *Bulletin* 1945 v 42, 469 found that an Italian preparation of neosarsphenamine (Neo I C I) had little effect on louse-borne relapsing fever in Addis Ababa Abyssinia. Charters however who used an allied arsenical preparation called "Neocal" at Sodda, Abyssinia found that after a dose of 0.6 gm. intravenously clinical improvement took place within 24 hours, spirochaetes could no longer be found in thick blood films after 8 hours, and no relapses occurred. He suggests the following possible explanations of the difference in the results: (1) Wohman's patients were probably treated later in the attack than the author's who were Gold Coast soldiers. (2) some of Wohman's cases, regarded as "first attacks" may have been relapses. (3) natives of the endemic district (Wohman's patients) may possibly respond less readily to the arsenical drug than new arrivals (Gold Coast soldiers). He thinks that the first explanation is the most important of the three. In his experience arsenical drugs have far greater effect on louse-borne relapsing fever than on the tick-borne form. J. F. Corson.

## LEPROSY

BECHELLI L. M. KEIL H & ROTBERG A. Resultados da lepromino-reação em países não endêmicos da lepra. (Nota preliminar) [The Lepromin Reaction in Countries where Leprosy is not Endemic.] *Rev Brasileira Leprologia* São Paulo 1945 Mar, v 13 No 1 21-4

BARGEHR DE LANGEN and others in the Dutch East Indies have reported positive lepromin reactors among apparently healthy individuals in contact with lepers contrasting them with recent arrivals who do not react. It is inferred therefore that the lepromin reaction is an indication of a prior latent infection with production of specific antibodies. Children removed at birth from their leper parents react negatively.

The authors have tested the Mantoux reaction and the early and late lepromin reactions in patients at the Skin and Cancer Unit of the New York Post Graduate Medical School and suffering from conditions other than leprosy. Twelve had been born and had lived for part of their lives in places with very low leprosy incidence. 36 had lived for a time in places where the disease was endemic. The results of each test are given in tables and the conclusions to be drawn from them are that a delayed lepromin reaction does not necessarily indicate a latent infection but may be regarded as allergy to the lepromin injected 3-4 weeks before. WADE has remarked on the positive reaction to lepromin in persons who had not been previously in contact with lepers and he explained this by saying that such persons can react allergically to Hansen's bacillus when they come into contact with it. From the results recorded in the tables the early reaction does not necessarily indicate either latent infection with leprosy or sensitization to lepromin, for it may occur in 6-12 hours. It is thought that tuberculosis is responsible for all but one of those tested who gave the early response were also Mantoux positive. The early lepromin reaction therefore must be regarded as non specific and due to sensitization to *Mycobacterium tuberculosis*.  
H Harold Scott

AMENDOLA F. A glândula lacrimal na lepra ocular [The Lachrymal Gland in Ocular Leprosy] *Rev Brasileira Leprologia* São Paulo 1945 Mar v 13 No 1 3-11 1 pl.

The lachrymal glands orbital and palpebral by continual secretion of tears when infected by leprosy constitute an important focus of infection. Bacteriological examination often shows these to be infected in leprosy and their extirpation thus removes one focus of infection. In patients where other eye lesions are present even though the glands do not appear to be involved removal of them is often followed by marked improvement of these other lesions. This last was observed in three of the 20 cases briefly detailed in this paper. Thus one a woman of 18 years had extensive keratitis of one eye and of one third of the other with photophobia and epiphora. she was very depressed about her eyes and all kinds of medical treatment had been tried ineffectively. Extirpation of the lachrymal glands was performed. histological examination of sections failed to reveal Hansen's bacteria. Nevertheless a few days later the patient presented herself without pain or photophobia, happy and cheerful and hopeful of complete cure. Two months after the operation the benefit was maintained. The author is hopeful that the operation may prevent much of the suffering and ultimate blindness which now afflict so many lepers.  
H Harold Scott

GRAU TRIANA J. Exploración de poder oxido-reductor de la piel en la lepra. [The Oxidation-Reduction Potential of the Skin in Leprosy] *Rev Sifilografía Leprologia y Dermatología* Marianao Cuba. 1945 Oct. v 2, No 3 154-8.



JULIÃO Oswaldo Freitas Contribuição para o estudo do diagnóstico clínico da lepra nervosa.

This book is reviewed on p. 265.

GONZÁLEZ PRENDES M. A. & IBARRA PÉREZ R. Duración de la lepra. [The Duration of Leprosy] *Rev. Sifilografía, Leprología y Dermatología* \* Marianao Cuba. 1945 Oct. v. 2, No. 3 175-9

Duration of illness in this disease is very difficult to assess as it depends on so many factors, among them the treatment adopted whether it is begun early or late whether it is carried out rigorously or half-heartedly whether the surroundings are hygienically sound, whether the general state of health of the patient is good the appetite faith in the success of treatment and other matters. JEANSELMÉ gives the duration as 10 to 20 years RODRIGUEZ up to 40 years MIRANDA from a study of 552 patients who died, gives "an average of over ten years" and many have stated it to be over 20 years and occasionally as long as 40 and even 50 years.

The authors have tried to assess the average duration from a study of 270 cases. They found that 43.3 per cent. discovered symptoms between the ages of 16 and 30 and 15.1 per cent. between 16 and 20 years. The average age at which they became ill was 25.7 years, and assuming that the incubation period was five years (a big assumption) the average age at first infection is given as 20.7 years. In 121 cases (44.8 per cent.) the average duration was 16-25 years (including incubation) and 62 were in the 16-20 years group. The average duration of the whole 370 worked out at 23.15 years (we give the authors figures they are not easy to reconcile with the details in the tables presented). As extremes, one patient died in three years and another after 56 years illness. The greatest number of deaths occurred between the ages of 36 and 45 years with an average of 43.8 years. *H. Harold Scott*

LEMA L. de S. & CERQUEIRA, G. de C. Terapêutica experimental da lepra pela soluthiazamida. Nota prévia [Trial of Soluthiazamide in the Treatment of Leprosy] *Publicações Médicas* São Paulo 1945 June-July No. 154 3 5-7 9-11 English summary

Soluthiazamide is p (γ-phenyl-propylamine) phenyl-sulphamido-thiazole-α-γ disulphonate of sodium. It is used in 45.3 per cent. solution, which contains 20 per cent. of thiazamide base. A 5 cc. ampoule contains 1 gm. of thiazamide. Most concentrated sulphonamides have a pH between 9 and 11.4 and thus degree of alkalinity causes eschars soluthiazamide has not this drawback. Trials with it for leprosy have been going on for 8 months this is too short a time for a definite appraisement of its therapeutic value but the results so far as reported by the authors are sufficiently promising to warrant more extensive testing.

Their clinical material comprised 100 cases, 50 with lepromata in a comparatively early stage and 50 adults with severe lepromatous forms and extensive involvement of the skin in whom chaulmoogra had proved ineffectual. The drug was administered intravenously each day except Sundays, for 3 weeks, the course being repeated after a week's interval the initial dose was 1 cc. which was increased gradually to 5 cc. and in adults to 10 cc. Those receiving more than 5 cc. were given also an equal amount of glucose solution.

The results observed so far comprise cicatrization of leprotic ulcers and of conglomerate lepromata, disappearance of lepromatous infiltrations and softening of subcutaneous nodules perforating ulcers of the sole sometimes

improved and ocular symptoms after a brief period of exacerbation showed considerable amelioration and had not relapsed during the time that patients were under observation the nostrils became clearer less obstructed crusts disappeared and respiration was freer

Examinations of the blood and urine were carried out systematically during the treatment. The red corpuscles were counted and the haemoglobin estimated before the treatment started and every ten days afterwards. If the red cells fell to 4 million per cmm. iron was given. If between  $3\frac{1}{2}$  and 4 million liver extract was ordered. If lower still soluthiazamide treatment was suspended and the anaemia treated until the blood returned to normal then it was restarted with small doses and gradually increased. If albumin or red corpuscles appeared in the urine the treatment was temporarily suspended. *H Harold Scott*

POSSOLO Helena. *As flacourtiáceas antileproticas.*

This book is reviewed on p 266

## HELMINTHIASIS

BURROWS R. B. A Survey of Intestinal Parasites in Natives in Dutch New Guinea  
*Amer J Hyg* 1945 Nov v 42 No 3 262-5

NIRO F. L. Papel de los helmintos en las llamadas apendicitis verminosas.  
[Worms found in so-called Verminous Appendicitis.] *BoI Inst Clin Quirúrg*  
Buenos Aires. 1945 May v 21 No 173 277-81 6 figs

OCKULY E. A. Bilharziasis of the Bladder (Vesical Schistosomiasis) *J Urology*  
1945 July v 54 No 1 39-45 1 fig [25 refs.]

This is a record of the first case of urinary schistosomiasis detected at the Army Air Forces Regional Station Hospital No 1 in Florida. The patient a sergeant aged 22 was infected in North Africa or Sicily was diagnosed cystoscopically as suffering from a tumour of the bladder and was invalided to the U.S.A. The correct diagnosis was there eventually established by cystoscopic biopsy and subsequently confirmed by the rather simpler procedure of urine examination which revealed eggs of *S haematobium*.

The patient was cured with Fouadim. The author discourses [at times loosely] on urinary schistosomiasis and stresses the possibility of other members of the forces being found to be infected on their return to the United States.

*A R D Adams*

KRAKOWER, C. HOFFMAN W. A. & AXLMAYER J. H. Granulación en la cubierta de los huevos de *Esquistosoma mansoni* (Experimentación con cobayos esquistosomizados y alimentados con una ración deficiente de vitamina C.) [Granulation of the Shell of the Ovum of *Schistosoma mansoni*. An Experiment with Infected Guinea-pigs fed on a Diet deficient in Vitamin C.] *Puerto Rico J Pub Health & Trop Med.*  
1944 June v 19 No 4 669-78 2 pls.

One hundred and thirty nine guinea-pigs each weighing 200-400 gm. were each infested with about 4 000 cercariae of *Sch mansoni*. They were then divided into five lots. Four were given the following diet deficient in vitamin C. Rolled oats 59 per cent. powdered skim milk 30 per cent. heated in trays to 10°C. for an hour 10 per cent. butter and 1 per cent. NaCl. Three of the lots

[March, 1949]

were given thrice weekly injections of ascorbic acid, the total weekly dosage being 3 g and 25 mgm. respectively. The other lot had no vitamin. The fifth group was fed on green food.

All those on a scorbutic diet died within a month or were killed at the end of that period, i.e. before oviposition had occurred. In these animals the parasite had undergone no change in growth or development. The same was observed in the group receiving 3 mgm. ascorbic acid weekly. Disintegrated ova were rarely seen in those receiving 9 mgm. Of 50 animals showing the ovular changes 28 lived for more than 5-6 weeks after being infested. The last one was killed after 109 days. Many of these guinea pigs showed signs of scurvy and in the 26 the schistosome ova seen in sections of tissue from the liver and lungs were disintegrating. The shells were swollen, sometimes laminated, eroded and granular and around them histocytes giant cells and perhaps lymphocytes eosinophiles and polymorphonuclears. In the last stages the shells became granular with greenish refracting granules single or grouped. To confirm these observations a lot of 12 guinea pigs ten weeks after infestation were gradually transferred from their green food to a scorbutic diet and 7-9 days after being on the latter they were passing ova with disintegrated shells and these increased in number till at the end of four weeks half the eggs seen in sections of the liver had disintegrated shells. Such ova were very rarely seen in those receiving 9 mgm. ascorbic acid weekly added to the scorbutic diet or a diet with insufficient antiscorbutic addition. Briefly the effect of a scorbutic diet on the number of eggs produced and the eggs themselves seemed to undergo a lytic process whereby the shell became granular while the surrounding tissue showed a certain degree of fibrosis.

HERNÁNDEZ MORALES, F. Schistosomiasis Mansonii Manifestations of the Large Intestine. *Puerto Rico J. Pub Health & Trop Med* 1943 June v 20 No 4 492-8 [Refs in footnotes] (Spanish version 499-506) H. Harold Scott

HERNÁNDEZ MORALES, F. & RUIZ CORDERO, G. Roentgenological Changes of the Small Intestine in the Presence of Schistosoma mansoni. *Puerto Rico J. Pub Health & Trop Med* 1945 June v 20 No 4 807-10 [Refs in footnotes]

ELIASBERG, K. H. Zur Symptomatologie Diagnostik und Therapie der Hymenocercose Bericht über 8 Erkrankungen und tabellarische Zusammenstellung der Fälle des Schistomsens seit 1910. [The Symptoms, Diagnosis and Treatment of Cerebral Cysticercosis. An Account of Eight Cases and a Table of Cases recorded since 1910.] *Ztschr. f. d. Neurologie u. Psychiatric* 1944 July 25 v 177 No 3 323-62, 8 figs. [Numerous refs.]

An article of much importance to all neurologists and not only to tropical practitioners. The author records in detail 8 cases of cysticercosis of the brain under his own observation and reviews a large number of cases reported in the last 34 years. The condition is very likely to be missed because the symptoms are not at all definite (see later) and even more because the suspected he urges the importance of bearing the possibility in mind by those practising in districts where it is liable to occur and by any medical man called upon to treat patients who have been stationed, or have lived in areas where the infestation exists.

At the author's clinic only 8 cases have been seen in the 12 years 1931-42 inclusive 6 in men and 2 in women. During that time some 20 000 patients have been seen among them 2,500 neurological cases of these there were some 900 with signs and symptoms of cerebral tumour so that there has been an average of one case of cerebral cysticercosis in every 125 of tumour.

There is no need here to detail the symptoms in each case there is a general type common to all in which the symptoms are those associated with hydrocephalus in the adult headache early and persistent especially occipital and extending down the neck giddiness nausea and vomiting. These symptoms are usually aggravated by head movement so the head is held steady as a rule fixed to one side and movement is restricted or carried out very cautiously. This goes by the name of the Bruns symptom. There may be affections of gait and of sensation but these are rare and not in any way characteristic psychically patients are mentally dull but often euphoric. The duration of illness is difficult to assess because many show neurasthenic symptoms for some years which may of course have no connexion with the symptoms psychic and other due to the cysticercosis. Also some patients have intervals of improvement when symptoms may almost be absent for varied lengths of time. In a table of 63 cases with cysticerci situated in the basal meninges the duration of symptoms is recorded as short several weeks to as long as 26 years in one case recorded by GUILLAIN PÉRISSON in 1927 [but not mentioned in the list of references]. Of these 63 forty (perhaps more) presented psychic disturbances of one kind or another. Others might be merely apathetic or show Korsakov's syndrome paranoia, depression or hyperaesthetic emotional states.

Diagnosis is not easy because symptoms are in general so vague. Rarely lumbar cysternal or brain puncture may result in finding fragments of a parasitic cyst. They tend early to calcify and then X-rays will reveal them. The cerebrospinal fluid may show 2-3 per cent. of the cells to be eosinophiles.

A favourite site for the cysts is the fourth ventricle. The author gives a list of 41 in which this was the case and in a few there was a combination of fourth ventricle and basal meningeal infestation. Information in this list includes the name of the author reporting the year of record the sex and age of the patient the chief clinical symptoms and the duration of the illness so far as this could be determined it ranged from a few days to perhaps 30 years. The ventricular cases are characteristically those which have an acute ending. The cysticerci are said to pass from the choroid plexus to traverse slowly the third ventricle and the aqueduct and, having increased in size are unable to penetrate the narrow slit like lateral apertures to the foramen of Magendie. They are usually monolocular rarely of the racemose type. If the cyst dies it becomes shut in by neuroglial fibrosis and then acts like a neoplasm. Pressure symptoms comprise a medium degree of papillary oedema on both sides but only a few patients have serious disorders of vision in a fair number there is slight paresis of the 3rd and 6th cranial nerves cerebellar ataxy is seen in about one-fifth of the patients epileptic attacks in one tenth but more in the basal meningeal cases than in those with ventricularly situated cysticerci. Operation is the only satisfactory line of treatment.

H Harold Scott.

ANDERSEN D. A. Hydatid Cysts. A Clinical Study of a Short Series. *Indian Med Gaz* 1945 Aug v 80 No 8 373-7

ROGER, H. Les kystes hydatiques du cerveau [Hydatid Cysts of the Brain.] *Méd Trop Marseille*. 1944 Mar-Apr v 4 No 2, 89-110 7 figs. on 4 pls. [Bibliography]

MUKERJI A. K. & SEN GUPTA, K. K. Effect of Heat and Light on the Ascaridol Content in Oil of *Chenopodium*. *Indian Med Gaz.* 1945 July v 80 No. 7 747-8.

MUKERJI and GHOSH [this *Bulletin* 1943 v 40 822] showed that when oil of *chenopodium* is kept at temperatures of from 70 to 93°F., whether exposed to light or kept in the dark its ascaridole content decreases. To find the best way of storing the oil the authors of the present paper made experiments in which they kept samples in glass-stoppered bottles for one year under various conditions of temperature and exposure to light, the ascaridole content being determined at 2 4 6 and 12 months.

The smallest amount lost was in the samples which were kept in subdued light at 65-75°F. and the authors conclude that oil of *chenopodium* is best stored in a cool place where the temperature does not rise above 75°F. and where there is protection from direct light.  
J. F. Corson

HERNÁNDEZ MORALES F. & DIAZ RIVERA, R. Poisoning by Carbon Tetrachloride and Oil of *Chenopodium*. *Puerto Rico J. Pub Health & Trop Med* 1943 June v 18, No 4 434-42. [Refs. in footnotes.] [Spanish version 443-51]

Three cases of poisoning by a dose of a mixture of carbon tetrachloride and oil of *chenopodium* are described. The patients were white Porto Rican labourers aged 31 36 and 35 years, respectively and the circumstances were similar in all. Each man took a mixture of 2 cc. of carbon tetrachloride and 1 cc. of oil of *chenopodium* [a well recognized therapeutic dose] in the morning on an empty stomach, and immediately afterwards took 60 gm. of magnesium sulphate. The first two men were admitted to hospital two days later and the third man three days later. In addition to the clinical examination, the urine and blood were tested at short intervals in the laboratory and the findings are shown in tabular form.

The symptoms were similar in all. An hour or so after taking the dose the patient had vomiting and diarrhoea with pains in the abdomen headache and general body pains and in two cases cramps in the arms and legs. Tenderness over the liver was present in all and two showed jaundice and enlargement of the liver the lower edge being palpable three fingerbreadths below the right costal margin.

The urine was scanty in amount in all three but showed only traces of albumin and few casts, and the specific gravity was very low. The reaction was acid. In the third case in which the effects of poisoning were the most severe the amount of non-protein nitrogen of the blood is given as 200 mgm. per cent. on the day after admission 300 mgm. four days later declining gradually to reach 40 mgm. on the 25th day after admission.

The patients were treated similarly. They were given a high carbohydrate diet calcium gluconate and glucose solution were administered intravenously and calcium lactate was taken by mouth. All recovered and were discharged from hospital on the 16th 19th and 27th days respectively after admission.

The authors quote the views of various authors on the mode of action of the drugs and remark that it is difficult to decide which of the two drugs caused most damage, but they think that carbon tetrachloride caused most of the symptoms.  
J. F. Corson

DOLCE F. A. & FRANKLIN J. E. Creeping Eruption. Results of Treatment with Fusidin. *Arch. Dermat. & Syph.* 1945 Sept. v 52, No. 3, 174-3.

"The results of treatment with fusidin of 14 patients with creeping eruption were unsatisfactory in all but 2 instances."

BUCHANS R. A. Filariasis in the Armed Forces. *J Urology* 1945 July v 54 No 1 59-61

Before the recent war Bancroftian filariasis was associated in the minds of most medical men chiefly with pictures of elephantoid scrota or limbs. The author states that these conditions result only from years of constantly repeated infection and that few if any cases will be encountered in men of the U.S. forces serving in the South Pacific area. He wishes to allay the anxiety inspired by inspection of the text book pictures by medical practitioners at home and by anxious relatives of which he says the end results on morale are terrific.

In actual fact the findings in men returned to the U.S.A. with a diagnosis of filariasis have been minimal and he observes that sterility does not result from the infection. He offers some observations on the aspects of filariasis from the urological standpoint.

A R D Adams

RAO S S. Filarial Infection in Dhamda (Drug District, C.P.) due to *Wuchereria malaya*. *Indian J Med Res* 1945 May v 33 No 1 175-6

Dhamda village is 21 miles north of the town of Drug Central Provinces India and has a population of 3 628. The author took thick blood films between 9 p.m. and midnight from 120 persons in February 1942 and found microfilariae of *Wuchereria malaya* in 16 (13.3 per cent). A survey of the village population at the time showed that there were 80 cases of elephantiasis of the legs or hands (2.2 per cent) but no cases of hydrocele, chyluria, lymph varix or elephantiasis of the external genital organs were observed.

During the period of the survey the following mosquitoes were prevalent in the village: *Mansonioides annulipes* [= *longipalpis*], *M. uniformis*, *Culex fatigans* and *Anopheles culicifacies*. All the big tanks were full of *Pistia stratiotes* and *Mansonioides* bred there. Among the mosquitoes dissected *Mansonioides annulipes* alone showed filarial infection and this therefore appears to be the most important local vector. [See also this *Bulletin* 1937 v 34 33. *Indian J Med Res* 1940 v 28 609.]

J F Corson

McMARTIN W J. Urological Aspects of Filariasis. *J Urology* 1945 July v 54 No 1 62-74 [16 refs.]

After brief and lucid accounts of the history, geographical distribution, aetiology, pathology, symptomatology, diagnosis, psychiatric aspects and treatment of Bancroftian filariasis the author cites six cases of the many he has seen in service hospitals in the U.S.A. illustrative of the distribution of the lesions as classified by HUNTINGTON, FOGEL, EICHOLS and DICKSON (*Yale J Biol & Med* 1944 v 16 529).

He ends with the following reassuring conclusions —

Filariasis has infected thousands of our armed forces located in the Pacific area.

The disease in these men is characterized by episodes of lymphangitis and lymphadenitis with the majority of the patients showing genital (scrotal) involvement.

Civilian urologists will be confronted with the problems of differential diagnosis of intrascrotal pathological changes caused by filariasis as well as intrascrotal pathological changes usually encountered in the United States.

There are many members of our armed forces who have filariasis and fear the onset of elephantiasis despite attempts of medical officers to dispel their fears. We can do a great deal to ease these patients' minds by educating them on the characteristics of the disease.

There is no specific drug in the treatment of filariasis. Removal of the patient to a temperate climate and away from the chance of more infection is most important.

"Rest, elevation of the affected parts and cold applications is the treatment of choice in episodes of exacerbations of the disease.

Research on the treatment of filariasis is constantly being carried out by very competent medical personnel of the Army and Navy. Excellent results of this work may be reported in the literature soon.

Much will be added to the knowledge of the pathology of early filariasis when and if complete post mortem examinations can be done on patients who have filariasis or who give a history of having had filariasis at some time during their life.

Filariasis will not become a public health problem in the United States.

"Permanent disability as a result of filarial infestation among our armed forces will be a rarity.

The Army and Navy Medical Corps have progressed rapidly towards eradicating this disease.

A. R. D. Adams.

ROSE, H. M. CULBERTSON J. T. & LIPMAN Miriam O. Antistreptolysin Titers in Cases of Filariasis with Recurrent Lymphangitis among Military Personnel. *J Clin Investigation* 1945 July v 24 532. [Summary taken from *J Amer Med Ass.* 1945 Nov 17 v 129 No. 12, 830-31.]

Rose and his co-workers determined antistreptolysin titers in the blood of 45 soldiers suffering from recurrent lymphangitis associated with filariasis contracted in the South Pacific. The titers were within normal limits in 39 of the 45 cases. The attacks of lymphangitis in these soldiers appeared to be due to allergic reactions to the parasitic infection. Secondary streptococcal infections were of little or no consequence as an etiologic factor.

WILCOX R. R. Genital Oedema in relation to Filariasis in the Gold Coast. *Brit J Tropical Dis.* 1945 Dec. v 21 No. 4 178-9.

Oedema of the external genital organs was present in 10 out of 875 African soldiers admitted to a hospital at Accra, Gold Coast between June and September 1944. Examination of the blood showed microfilariae of *Loa loa* in 5 and microfilariae of *Acanthocheilichneumon perstans* in 1. Microfilariae of *Onchocerca volvulus* were found in the skin of 1 man who had also a guinea-worm in the scrotum. Some of the 10 men gave a history of having had several attacks of genital oedema.

Treatment was by means of a suspensory bandage and in 4 cases the swelling subsided within a week. One was operated on for elephantiasis of the penis and scrotum. [The incidence of filarial infection among the other 775 soldiers is not given.]

J. F. Corson.

BONNET R. Réflexions sur un cas de méningite aiguë à *Microfilaria loa*. [A Case of Acute Meningitis due to the Microfilaria of *L. loa*.] *Méd Trop Mar Indes.* 1943, July-Aug v 3 No. 4 273-7.

WANSOY M. & HENRIARD C. Habitat et comportement larvaire du *Simulium damnosum* Theobald. [Habitat and Larval Development of *S. damnosum*.] *Rec Travaux Sci Méd Congo Belge* 1945 July No. 4 113-21.

This gives a detailed account of the ecology of *Simulium damnosum* in the neighbourhood of Léopoldville in the Belgian Congo. The biting of these

insects constitutes a serious nuisance during the months of September to January (i.e. the start of the hot season) *S. damnosum* is also the vector of *Onchocerca volvulus*

The adult females migrate to the town from the rapidly running sections of the river by the way of shaded water-courses. They commonly migrate for several miles (45 miles is quoted as a maximum). Breeding goes on in various locations in the rivers the larvae and pupae being attached to stones submerged plants and wicker work fish traps. A sudden change in water level causes a high mortality but a gradual rise or fall allows the larvae to migrate to a suitable situation. The life-cycle from egg to adult takes about nine days and the adult female lives about three weeks. In certain regions *S. damnosum* is frequently parasitized by microsporidia this causes a substantial mortality

Kenneth Mellandby

WANSON M. HENRARD C. & PEEL E. *Onchocerca volvulus* Lenckart. Indices d'infection des simuliés agressives pour l'homme. Cycle de développement chez *Simulium damnosum* Theobald. [O *volvulus* Indices of Infection of *Simulium* and Cycle of Development.] *Rec. Travaux Sci. Méd. Congo Belge* 1945 July No 4 122-38 8 figs. on 1 pl.

*Simulium damnosum* and *S. albivirgatum* both attack man in the Belgian Congo but only *S. damnosum* is of importance as a vector of *Onchocerca volvulus*. The population of fishermen living near the rivers in which the vector insects breed is heavily infected (up to nearly 100 per cent) and 15 per cent of *S. damnosum* captured from their villages were infected. In villages five miles away from the breeding sites 65 per cent of the people and 8 per cent of the *Simulium* were infected. Further afield the infection rate in both man and insects declined still more.

Adults of *S. damnosum* have been kept alive in the laboratory for over a week in sufficient numbers to demonstrate the whole cycle of *O. volvulus*, which takes six or seven days.

Kenneth Mellandby

NETTEL F. R. Contribución al estudio de la distribución de los simúlidos en el estado de Chiapas. [The Distribution of Simuliidae in the State of Chiapas.] *Medicina Mexico* 1945 Nov 10 v 25 No 495 455-9 1 fig. English summary

13 505 simuliids were collected in 256 localities in the south of the State of Chiapas, where onchocerciasis prevails. In the mountainous regions the captures were made on man and near the coast on animals. In places where onchocerciasis is more prevalent *Simulium ochraceum* was found in greatest proportion being followed by *S. metallicum* and *S. callidum*. The other species were collected in small numbers not constituting a plague like the former

CLAPHAM Phyllis A. On some Characters of the Genus *Trichuris* and a Description of *T. parvispicularis* n. sp. from a Cane Rat. *J. Helminthology* 1945 v 21 Nos. 2/3 85-9 13 figs

SCHUFFNER W. Die Bedeutung der Staubinfektion für die Oxyuriasis. Richtlinien der Therapie und Prophylaxe. [The Importance of Dust-borne Infection in Enterobiasis. Rules for Therapy and Prophylaxis.] *Munch. med. Woch.* 1944 Aug 11 v 91 Nos. 31/32 411-14 [Numerous refs.]

Infestation experiments on seven persons (doctors and students) enabled SCHUFFNER and SWELLENGREBEL to show that eggs of *Enterobius* which had dried for three days and longer in room dust retained their full



powers of development. Six out of the 8 subjects passed worms after 36 to 53 days—that is to say the shortest time required before worms were passed was 36 days and the longest 53 days. Thus dust-borne eggs are a source of infestation [cf also CRAM this Bulletin 1943 v 40 618].

The large numbers of eggs found by Schliffner and Swellengrebel [this Bulletin 1945 v 42, 924] in the dust of a school dining hall leaves no doubt of the importance of this source of infestation.

Eggs may get into the dust in various ways. LEUCKART thought that the eggs dry with the faeces because the female worms lay their eggs on the outer surface of the faeces—but it is doubtful whether these eggs play any part in the distribution of the worms. Most of the faeces are deposited in the closet and do not dry. The eggs in the very small amount of faeces deposited in the outer world are so much diluted by the atmosphere that hardly one of them will find a host. The main source of eggs in dust is the anal region which is also the main source of finger infection. From the anal region eggs pass into the air not singly but in clusters.

Many eggs which pass into the unenclosed atmosphere are lost or fail to develop—but within enclosed spaces the air can carry a wide variation of numbers of eggs. In one school studied by the author the number of eggs found on about 10 sq decimetres (q d.m.) (roughly 1 sq foot) of surface was 119 in a large dining hall, 305 in classrooms and about 5 000 in the much smaller closets. The size of the room is not the only factor which affects the density of eggs found. SMALT (*Nederl Tijdschr v Geneesk* 1944 p 20) found that the egg content in female closets was greater although the worm infestation of the females was not higher than that of the males. Doubtless dissemination of eggs is favoured by the movements of female clothes.

The spaces just mentioned are, however used only for a short time. There is a much smaller air space which is used for half the life of the infested person namely the air space under the bed clothes. This has been studied by OLESTKOFF (*Russ. J Tropenmed u med u vet Parasitenk* 1929 p. 395). This space is an important source of dust borne infestation for the eggs are disseminated night after night by the movements of the sleeper and can often enter the nose and mouth in considerable numbers. This is especially a risk for males who tend to draw the bedclothes over their heads more often than females do and this may explain why males, in spite of all precautions and repeated drug treatment are not freed from their infestations. Eggs are also distributed from the bed into the air by bedmaking.

Dust borne infection plays an important part in the epidemiology of enterobiasis. It does not cause heavy infestations which arise from finger infestations only but it introduces enough eggs to cause repeated light infestations. Finger infection may be added to it and then severe enterobiasis may arise. It is important to differentiate between these two kinds of infestation. The hypothesis of an enterogenous development of *Enterobius* within the alimentary canal has been suggested to explain repeated infestations and failures to cure but dust-borne infestation can explain these more simply and equally well.

Schliffner's own experiments show that in all the persons studied by him, the infestations, which lasted 12 to 27 days, ceased without treatment. The same result appears to have been obtained in the twelve experimental infestations with fresh eggs recorded in the literature [no refs. are given], although this was not always explicitly stated. In one person only experimentally studied by v DRIGALSKI and KOCH, (*Dtsch. med. Woch.* 1925 p 309) did the infestation reappear after nine months, in spite of every care. In this instance dust-borne infection was responsible for the reappearance of the infestation. Without it *Enterobius* dies out. In the author's experience its length of life is 37 to 83 days.

Preventive measures should be based upon a distinction between management of the individual suffering from active enterobiasis and general measures directed against carriers who exhibit inactive (latent) enterobiasis (see HAMBURGER *Munch med Woch* 1943 p 723). For latent enterobiasis there is no treatment hygiene thereby acknowledges its weakness we can only try to limit the degree of the infestation. In active enterobiasis the intensity of the irritation may vary not only with the number and vigour of the worms but also with the sensitivity of the subject some subjects who are not ticklish may suffer little from even an active enterobiasis (e.g. one of the persons used experimentally by Schuffner). In active enterobiasis also dust borne infestation is of capital importance. It has hitherto been much underestimated. It provides a gap in the control plan which is responsible for failures in treatment. It is useless to enforce severe hygienic rules if dust borne infestation is not also controlled. The rule is to treat the symptoms only and to do this by the simplest means. Schuffner recommends for this purpose small enemas (*Einläufe*) of 30 to 50 cc. of water for the temporary appeasement of the anal irritation. These wash out the worms in the anal area. Inspection of the rectum at the height of the irritation shows active worms in the anal folds. When these are removed the irritation ceases at once. The view of LORENZ (*Med Klin* 1925 p 95) that the irritation is due to larvae of *Enterobius* is not correct because the larvae are too small and Schuffner saw them hatch in the anal region only very exceptionally. Schuffner agrees that some larvae may hatch here and creep back to continue their development in the intestine as LANGHANS (*Arch. Kinderh* 1926 v 77 27) suggested but he has as yet not enough evidence to prove it this is at any rate not true enterogenous development but merely avoidance of the usual entry by the mouth.

Small enemas are in Schuffner's experience sufficient to remove the worms present in light infestations often there is only one worm present. High enemas given with the object of getting at the immature worms higher up in the intestine are not only quite superfluous, but are also often very disturbing to the subject. These worms are better eliminated by anthelmintics. No known substance has all the properties of an ideal anthelmintic. The author discusses and apparently recommends gentian violet (see also CRAW *this Bulletin* 1943 v 40 618). Danish use of this drug is similar to its use by American workers. Reckoning the life of *Enterobius* as from 37 to 53 days (see above) Schuffner concludes that if eggs appear in less than 37 days after anthelmintic treatment (or adopting LENTZ's (*Zent f Bakt* 1935 v 135 156) estimate of the length of the life history in less than 25 days) the anthelmintic has failed. If eggs appear between 37 and 53 days after treatment the drug may have eliminated the worms present but a new infestation (e.g. a dust borne one) may have occurred. If eggs appear after the 54th day after treatment a new infestation must have occurred even if the drug has eliminated all the worms originally present.

Known anthelmintics however must not be expected to give a permanent cure because dust borne infestation is so difficult to control. The author deprecates the use of aperients, which are he thinks, practically never justified. For prophylaxis against finger infection Schuffner recommends increased cleanliness of the hands and washing of the anal region immediately after rising in the morning. This gets rid of eggs before the daytime clothes are put on and the child remains all day in a personal environment more or less free from eggs. Washing after each stool does some good but does nothing directly against the worm. The practice of it is based on the faulty observation that eggs are laid in the intestine and are taken up only from the stool. Schuffner and Swellengrebel found, on the contrary, that eggs are laid only very exceptionally in the intestine.

The wearing of closely-fitting bathing drawers at night is a useful means of prevention of soiling of the hands although eggs, as LENTZE [this *Bulletin* 1938 v 33 121] showed can easily pass through the most closely woven materials. The drawers prevent however the picking up of eggs by scratching and this justifies their use they can convert an active into a latent enterobiasis and they hinder distribution of eggs in the bed and thus prevent dust borne infestation under the bedclothes. Loose night clothes help this kind of infestation.

The precautions so far mentioned may practically close the finger-mouth route of infection, but they only partly restrict dust-borne infection which is especially important at night in bed. KOCH LENTZE and others think that *Enterobius* ceases to migrate out from the anus after midnight, so that a second washing of the anal region after midnight may do good this is, however troublesome for the mother and may for that reason alone, not be justified. Another measure is to close the anus with suppositories, ointments etc. This together with the wash immediately after rising in the morning will almost completely prevent dust-borne infection.

The author thinks that many textbook measures are unnecessary they may also lead to threadworm neurosis. Among these he includes treatment of the members of the family suffering from latent enterobiasis, daily changes of bedclothes and underclothes and sterilization of these keeping the nails short, change of diet stool examinations, high enemas and purges. Dust-borne infection cannot be entirely eliminated, so that it is useless to aim at permanent cure by such strict rules. The author is discussing enterobiasis in Amsterdam, where he says that 100 per cent. of children are infested. When dust-borne infection is not a risk, the author recommends the simple measures given above, because in 5 to 7 weeks the worms will naturally die out. G. Lapege

GAASE, A. Ueber die Verwendbarkeit der Komplementbindungsreaktion zum Nachweis der Trichinose. [On the Value of the Complement Fixation Reaction for the Diagnosis of Trichinosis.] *Munch. med. Woch.* 1944 Aug 25 v 91 Nos 33/34 440-41 [14 refs]

The occurrence of a localized outbreak of trichinosis in Germany in 1943 enabled the author to test further the value of the complement-fixation reaction tested by him and others in earlier work. The illness was not severe and *Trichinella* could not be found by meat inspection. The symptoms were more subjective than objective. Within seven weeks the sera of 110 members of the Wehrmacht were sent to Gaase to be tested for trichinosis. Of these 82 (74.5 per cent) were feebly or strongly positive. This percentage of positives seemed to be low but only one sample of 17 out of the 28 negative sera was sent for examination, so that probability of a positive reaction was not great. It was, therefore, all the more striking that in some subjects the reaction was positive shortly after the appearance of the symptoms [the author does not say how long after]. The limited amount of antigen available prevented the use of daily tests to detect the earliest time when positive reactions appeared, but it can be said that the number of positives would have been higher if this point could have been systematically investigated. The value of the complement fixation reaction for the diagnosis of early cases of light *Trichinella* infections was, however demonstrated. In three subjects the reaction was positive or lightly positive on the second day, which is an earlier date than that observed by Gaase in experiments on animals. By the seventh day the number of positives reached 13 the first strongly positive reaction occurring on the fourth day. The author does not however claim any finality for these figures. He used an antigen prepared from swine.

Eosinophilia is an almost constant symptom of trichiniasis but the degree of it does not indicate the degree of the infestation nor does the degree of prevention of haemolysis in the complement fixation reaction indicate the severity of the *Trichinella* infestation. For these reasons the author enquired whether there is any relationship between the eosinophilia and the antibody content of the subject's blood. No such relationship could be found. In most subjects with a strongly positive complement fixation reaction the number of eosinophils was markedly increased but some giving lightly positive reactions had 30 to 40 per cent of eosinophils and conversely others giving strongly positive reactions had 0 to 7 per cent of eosinophils. There is little evidence to decide whether the eosinophilia or the complement-fixation reaction is the more reliable for early diagnosis. Experimental work on animals has enabled the author to demonstrate by means of the complement fixation reaction the presence of a *Trichinella* toxin in the brain [see this *Bulletin* 1945 v 42 481 and the literature there quoted].

The successful use of the complement-fixation reaction for the detection of light infestations of man with *Trichinella* suggests that similar light infestations occur in animals. This consideration together with the fact that outbreaks of trichiniasis occur in areas in which careful inspection of meat for *Trichinella* has failed to detect it seems to justify the supplementing of meat inspection with complement fixation reactions done upon the swine. *G. Lapege*

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### DEFICIENCY DISEASES.

GILLMAN T & GILLMAN J. Hepatic Damage in Infantile Pellagra and its Response to Vitamin, Liver and Dried Stomach Therapy as determined by Repeated Liver Biopsies. *J Amer Med Ass* 1945 Sept 1 v 129 No 1 12-19 8 figs. [Refs in footnotes.]

In this paper the authors describe in detail the damage found in liver biopsy specimens (taken according to a modification of the technique of Iversen and Rohohn [see this *Bulletin* 1945 v 42 1045]) from African children suffering from the type of infantile pellagra which is so severe that 50 per cent of them die though treated with vitamins and a satisfactory diet. The condition found and the clinical signs together with details of the authors' new and successful treatment with a dried stomach preparation are referred to in previous papers abstracted in this *Bulletin* 1944 v 41 1057 1945 v 42, 748 1946 v 43 9.

The present communication is based on a study of 20 livers. From the pathological point of view these fall into three categories. In the first there is enormous accumulation of fat in the liver cells in the form of single large pale-staining globules filling the entire cell. In the second (less serious) form almost all cells contain multiple coarse droplets of fat. In the third the cells contained dust-like particles of fat.

The authors discuss the results of treatment again emphasizing the value of dried stomach, even in the restricted amounts they were able to give. They think that the presence of large amounts of fat in the liver and in the stools though the diet of the patients had previously consisted largely of carbohydrate, and though there was little fat elsewhere indicates that carbohydrate is converted in the body to fat but that utilization of the fat is deficient and that it is excreted into the bowel or deposited in the liver cells. Vitamin treatment may not only be useless it may actually be harmful and it is known that large doses of nicotinamide produce fatty infiltration in the livers of rats. Other workers have noted the beneficial action of liver therapy in pellagra but in

comparison with the authors' results with dried stomach, the action of liver is slow and incomplete. They stress again their opinion that dietary imbalance may initiate the disease, producing secondary changes which are not susceptible of cure by administration of vitamins.

The African, in the Johannesburg area from which the authors write, exists in poor economic conditions and his liver is subject to repeated insults of this kind. It is likely that the known high incidence of cirrhosis and of primary hepatic carcinoma are due in no small measure to this chronic malnutrition.

Charles W. Coombs.

### SPRUE.

MAEGRAITH B. G. ADAMS A. R. D. HAVARD R. E. KING J. D. & MILLET R. F. Carbohydrate Absorption in Sprue. *Lancet* 1945 Nov 17 635 2 figs.

In the course of experimental observations on cases of sprue the authors investigated the absorption of glucose and fructose—the former is absorbed from the small intestine mainly after phosphorylation ("the process of introducing the trivalent PO group into an organic molecule" *Dorland's Med. Dict.*) while fructose is absorbed chiefly by simple diffusion through the intestinal mucous membrane.

After each patient had taken 100 gm. of sucrose by mouth the glucose and fructose levels in the blood were estimated every half-hour for 2½ hours. In the active cases of sprue the glucose curve was flat, the maximum rise seldom exceeding 20 mgm. per 100 cc. above the fasting level—the absorption was "of the same order as that of fructose." The fructose absorption curve was always within normal limits. Hence in these cases of active sprue the absorption of glucose was much reduced while that of fructose was unaffected. The reduction of glucose absorption is considered to be due to failure of phosphorylation in the small intestine.

Certain substances are known to be able to inhibit phosphorylation in the small intestine and magnesium, *in vitro* plays an important part in phosphorylation. The authors therefore estimated the plasma levels of Ca and Mg in their patients—the Ca levels showed little difference from the normal, but the Mg level was low in two patients (0.75 mgm. and 1.2 mgm. per 100 cc., respectively) who were acutely ill and had tetany at the time. In these two patients no direct relationship between the recovery of the carbohydrate absorption and the return of the Mg levels to normal was observed. In other acute cases without tetany a low Mg level was not found. J. F. Corson.

SINGH, B. Fatty Diarrhoea. A Report on 28 Cases. *Indian Med. Gaz.* 1945 Aug. 80 No 8, 388-90.

The patients, chiefly non-vegetarian Muslims, were admitted to a malnutrition ward in an Indian military hospital after periods ranging from 4 to 36 months (the majority within one year) in the forward areas.

The severity of their complaints could be classified into severe, moderately severe and mild. The manifestations essentially consisted of looseness of the bowel (3 to 13 motions in 24 hours), griping pains, vomiting and retching after meals, weakness and wasting, and in a few cases, "feverishness." The stools were pale, copious, of porridge-like consistency and slightly frothy, and contained 50 per cent. of fat, the ratio of split to unsplit fat being about normal.

All the men complained of soreness of the tongue at some time during their stay in hospital. Their red cell counts and haemoglobin content were not grossly abnormal in 9 cases where a fractional test meal was done it revealed hypoaclidity or achlorhydria.

The treatment included attention to diet and administration of drugs including dilute hydrochloric acid, nicotinic acid and the sulphanilamide drugs the latter controlled the diarrhoea while they were being taken but it recurred on their cessation if the general condition of the patient had not materially improved. Small repeated blood transfusions were given in a few cases without obvious benefit.

The author attributes the condition to restriction in food intake added to debilitation consequent on dysentery, a vicious circle thus being set up. The sulphonamides were of benefit in breaking the circle and restoring a more normal equilibrium from the sprue like state (para-sprue) into which the cases had declined.

HERNÁNDEZ MORALES F. Gastroscopic and Rectosigmoidoscopic Observations in Tropical Sprue. *Puerto Rico J Pub Health & Trop Med* 1944 Dec. v 20 No 2 257-67 [Reis in footnotes] [Spanish version] A R D Adams

Sixty-one gastroscopic examinations were performed on 36 sprue patients during the acute diarrhoeic stage and after liver extract treatment had been given for varying periods. In 55 per cent. atrophic changes were observed in the gastric mucosa. Practically all showed acute glossitis with absence of the papillae though following liver treatment the tongue showed great improvement. Sixteen were examined after treatment and in 10 the appearance of the gastric mucosa was restored to normal.

Recto-sigmoidoscopic examinations undertaken during the acute diarrhoeic stages revealed several types of lesions such as atrophic patches oedema friability purpuric spots and superficial inflammation.

Gastroscopic examination in sprue is the only available method of studying the changes in the gastric mucosa in this disease. It is once more stated in confirmation of the views of OLLEROS (*Puerto Rico J Pub Health & Trop Med* 1938 v 13 503) that the atrophy of the gastric mucosa is more intensive in pernicious anaemia than in sprue. P Manson Bahr

RODRIGUEZ MOLINA R. Sprue in Puerto Rico—Ten Years Later. *Puerto Rico J Pub Health & Trop Med* 1943 Mar v 18 No 3 314-40. [Spanish version 341-63.]

For the purposes of this study the sprue syndrome is held to be a chronic deficiency state characterized by its insidious onset chronicity of symptoms, progressive development of gastro-intestinal disturbances—mainly dyspepsia, soreness of the tongue and mouth meteorism and diarrhoea. The stools are usually liquid foamy greyish foul smelling voluminous and fatty. Stomatitis atrophic gastritis and recto-sigmoiditis are important findings. A macrocytic hyperchromic type of anaemia with a megaloblastic marrow accompanes about 90 per cent. of the cases. Loss of weight occurs in the same percentage of cases fever in about 40 per cent.

The symptoms of sprue may appear and become fully developed in the course of a few weeks but more usually a few months as the chronicity of symptoms is typical. This symptom complex may continue if untreated for several years before death ensues. Relapses are common, but spontaneous remission of gastrointestinal symptoms or of the anaemia are rare.

The rapid loss of weight and strength is associated with intestinal hypermotility with resulting malabsorption, and chronic and progressive starvation. Derangement of the metabolism of fats, carbohydrates and proteins is closely related to the failure of the absorptive intestinal function, and is believed to be intimately linked with the clinical picture of the syndrome.

This deficiency state in sprue is amenable to replacement therapy and symptoms can be cured by liver extract. The group studied comprised 51 males and 49 females, ranging from 12 to 78 years of age the mean age for the group being 40.14 years. There were 87 white and 13 coloured individuals among the latter were two full blooded negroes the others being mulattoes. Ninety-eight persons were natives of Porto Rico. With few exceptions the individuals were indigent and, when first examined, presented the fully developed picture of the sprue syndrome. The liver extract employed for intramuscular injection was prepared according to instructions given by W. B. CASTLE. This is a crude unconcentrated product from 343 Liver Powder Lilly and its efficacy for sprue and other macrocytic anaemias had been demonstrated. One cc. of this extract was equivalent to about 5 gm. of fresh liver. In the out-patient department it was given intramuscularly in doses of 5 to 10 cc. usually 5 cc. three times a week. Injections of 5, 8 and 10 cc. were often given daily in the wards. One individual received as much as 20 cc. intravenously daily. Whenever possible, reticulocytes were counted daily during the first two weeks of liver therapy. Wintrobe's haematocrit was employed to determine the volume of packed cells and a Newcomer Klett haemoglobinometer to estimate the haemoglobin in grammes and percentages. The diet prescribed, that of Ashford, was of low residue, high protein, low fat and low carbohydrate which assured assimilation even in presence of diarrhoea. In practice it included certain Island carbohydrate foods such as plantains, bananas *yandias* (a tuber similar to potato). The diets supplied from 1,500 to 2,000 calories per day.

Of the drugs taken orally the chief was a digestant of hydrochloric acid and pepsin and a small amount of strychnine. Another preparation contained tincture of opium prepared chalk and bismuth subcarbonate used for stubborn diarrhoea.

A table has been compiled of the number of deaths from sprue per 100,000 of population in Porto Rico during the decennial period 1928 to 1938. For the purposes of comparison deaths from other anaemias are also shown. In 1928 there were reported 88 deaths from sprue with a rate of 5.9 per 100,000. In 1938 the total number of deaths reached 103 and the rate 5.6 per 100,000. In white individuals the age groups showing the greatest number affected were 20-29 for females 20-29 and 40-49 for males. Twenty-six white males or one-half of the male group were affected between the ages of 20 and 50. There were 11 white women in the 20-29 group a higher number than in any other. This is significant as indicating that sprue attacked women most often during the period when pregnancy was most likely to occur and that its onset occurred not during pregnancy but after delivery. In the coloured group the largest number of females (3) fell in the 20-29 group of the 6 males there were two in each of the three groups between ages 20 and 50.

A total of 75 white and coloured individuals were discharged as improved and did not return during the ten-year period 1931-1941. The average duration of treatment was three years, with a range of one month to ten years, and the average hospital sojourn for 27 cases was 40 days.

The number of relapses was generally less in patients below 40 years of age. Upper respiratory infections were responsible for the greatest number of relapses next in order were dietary indiscretions. Cessation of liver therapy was also a cause.

The earliest indication of improvement under liver therapy was rapid and progressive disappearance of the lingual and buccal lesions accompanied by change in the appearance of mouth lesions. On diet treatment alone however this process was delayed for several weeks nor were all the papillae completely regenerated. The return of the long lost appetite was taken as an early indication of improvement. Relief of gastrointestinal symptoms was not apparent until a later date. It is believed that improvement was more rapid under liver and diet than with liver alone. Under combined liver and diet therapy the number of bowel movements might diminish as early as the second or third week. It was observed that any indiscretion in the diet even in those who were symptom free always resulted in a change in the appearance and frequency of the stools.

A rise in reticulocytes may be taken to mark the earliest indication of blood regeneration following liver therapy. The peak of this increase usually occurred from the fifth to twelfth day. When the red cells were more than three million the reticulocyte count was rarely higher than 10 per cent. As a rule the proportion of reticulocytes became normal (1 to 2 per cent) by the end of the second week. In general the reticulocyte peaks were lower in sprue than in pernicious anaemia. Changes in the morphology of the red cells such as anisocytosis and poikilocytosis were greatly diminished during the first few weeks of treatment but might persist for months particularly when macrocytosis was present.

In about 50 per cent of cases the mean corpuscular volume rose shortly after administration of liver extract as the amount of cells and their packed volume increased.

The leucocyte count if low usually returned to normal between the fourth and fifth weeks of treatment and the differential count also returned to normal. Macrocytosis of leucocytes disappeared promptly in the majority of cases. Low platelet counts returned to normal but not before the third or fourth weeks of treatment.

The amount of liver extract required to maintain a person with a high threshold requirement in good health once a full remission of symptoms had occurred varied widely with different individuals. The erythrocyte and haemoglobin responded rapidly but normal or subnormal levels were maintained for longer periods in individuals below forty years than in those over this age. In the older age groups clinical improvement with disappearance of gastrointestinal symptoms was frequently observed in association with subnormal blood levels.

The opportunity for observing permanent cures in sprue is lacking. It is known that of the 75 individuals discharged as improved, 65 have apparently remained well after five years without treatment.

Liver extract was given to one individual daily by the intravenous route in 10 and 20 cc. doses. No reaction, save pyrexia of 103°F resulted, but clinical and haematological improvement was no more effective nor did it appear any sooner than when liver was administered intramuscularly.

P. Manson Bahr

RODRIGUEZ MOLINA R. Sprue in Puerto Rico. A Clinical Study of 100 Cases. *Puerto Rico J. Pub Health & Trop Med* 1941 Dec v 17 No 2, 134-51 2 figs. [Spanish version 152-68]



## HAEMATOLOGY

BERG W. N. Blood Cell Counts: their Statistical Interpretation. *Amer. Rev. Tuberculosis* 1945 Sept. v 52, No. 3 179-220 12 charts. [28 refs.]

The main purpose of this very heavy and careful piece of work, which was undertaken for the Committee on Evaluation of Laboratory Procedures, is to describe the statistical aspects of blood cell counting so that any worker can make his own tests of significance by reading the tables provided. Taking as an example the red cell count the author first shows the variability that may occur by chance in making repeated counts of a single dilution of blood. For instance if 1 000 correct counts were made each on 80 squares, and the mean number of red cells were 300 the individual counts would vary between 248 and 352. This variability is due to chance or purely accidental variations in the way the red cells stream across the squares in the chamber. The majority of the counts would lie in a narrower range two-thirds approximately being between 283 and 317 but wider deviations will inevitably occur with some frequency. In practice this variation will be increased by variations in chamber size and in dilution pipettes. Thus the range of observed counts round the mean of 300 will be increased under normal conditions of careful routine from the 248 to 352 (above) to 224 to 378 two-thirds approximately lying between 275 and 325. The author briefly tabulates the frequencies with which counts would be expected to occur in this way round mean values from 200 to 800 and such statistical expectations have been found to be in accordance with observations.

The first problem arising then is to decide what information is obtainable from a single red cell count. Given, for instance a count of 464 on 80 squares, this result could come from a patient with only 372 or as many as 600 cells though most infrequently in either case. It might well arise from a patient with a real count lying anywhere between 400 and 540 a wide range. The table provided shows the possible limits for different observed counts. The second problem concerns the method to adopt in determining that a single chamber count has been made correctly. One such method is to count the cells separately in each of five groups of sixteen squares note the largest difference that occurs between any two of these five totals and from the table provided see whether such a difference is likely or unlikely to have occurred by chance. If the difference is unlikely error should be suspected. A second method is to compare the actual with the theoretical Poisson distribution, but this is laborious in practice.

The third problem is to determine how large a difference between two consecutive red cell counts on the same blood may be due to random sampling. A table of ranges is provided to show the extent to which two such readings may be expected to vary by chance. Alternatively from another table the ratio of the difference between the two counts to the standard deviation may be calculated. If the difference is greater than three times the standard deviation the probability that both counts were correctly obtained on the same blood is very small. Using this method, the author gives clear examples of its application in three situations—(a) counts on the same dilution. (b) counts of different dilutions of the same puncture. (c) counts derived from two punctures.

The fourth problem is whether two counts are better than one. If the first count happens to be close to the true value chance will place the second count further away making their mean a poorer estimate than the first count alone. Conversely if the first count is far from the truth chance will place the second count nearer and the mean will in this case give a better estimate. Since the investigator cannot tell which situation he is facing, the mean of two counts

cannot be depended upon to furnish a better estimate than either one alone. For practically all other purposes two counts are better than one.

A similar treatment and discussion is given to white cell counts and the neutrophil count the latter being applicable to other differential counts so long as they exceed 5 per cent of the total count. A table is given for estimating the amount of variation that may occur by chance for differential counts in which the observed percentage is less than 5.

[It is not possible in an abstract to reproduce the tables and explanatory matter in this paper which should be consulted in the original.]

A Bradford Hill

ENGLISH R B Sickleaemia occurring in Africans in Northern Rhodesia. *South African Med J* 1945 Nov 24 v 19 No 22 431

Sickleaemia is present in 17.52 per cent of African males employed on the copper belt of Northern Rhodesia. No significant difference in the incidence among healthy and unhealthy subjects is noted.

ROBINSON G A Rapid Method for detecting the Sickle Cell Trait *Trans Roy Soc Trop Med & Hyg* 1945 Dec v 39 No 3 264

The ferment broth used by NEUDA and ROSEN (this *Bulletin* 1945 v 42 825) in their rapid method for diagnosing sickle-cell disease is really a mixed culture of intestinal organisms. The author has used broth cultures of various bacteria—*Pseudomonas fluorescens* *Bact coli* *Staph aureus* *B subtilis*—for the rapid production of sickling of the erythrocytes. The presence of living bacteria is necessary as heating the cultures at 60°C for 1 hour filtering through Seitz Disk EK/3 or Pasteur-Chamberland Candle L3 or killing the bacteria with alcohol produces inactivity while suspensions from an agar culture are active without further incubation. *Method*—A drop of a 24- or 48-hour-old culture previously tested for its activity against known sickling corpuscles is placed on a slide and a smaller drop of finger blood mixed with it covered with a cover glass and examined under the microscope. In cases with the trait or with active sickle cell anaemia sickling of the corpuscles begins to show in from 1 to 5 minutes in most cases 70 to 90 per cent of the corpuscles being sickled in 15 minutes.

J F Corson.

WINSOR, T & BURCH G E Sickle Cell Anemia, "A Great Masquerader" easily recognizable with Routine Use of Diagnostic Parameter *J Amer Med Ass* 1945 Nov 17 v 129 No 12 793-6 4 charts.

Since sickle cell anaemia is such a great imitator and because it may remain so subtle it is necessary as a routine to study the blood for sickle cell anaemia in all negro patients. This can conveniently be done by the routine diagnostic use of the parameter [described by WINSOR & BURCH see this *Bulletin* 1945 v 42 484] such a search in 512 consecutive negro patients showed 27 (4.4 per cent) to have sickle cell anaemia. Two methods may be used in performing the test one employing CO<sub>2</sub> (diagnostic parameter  $\Delta_1$ ) and the other venous stasis (diagnostic parameter  $\Delta_2$ ) to produce retardation of the rate of the erythrocyte sedimentation.

In the second method a sphygmomanometer cuff is applied to the arm and a pressure between the systolic and diastolic blood pressure is sustained for 6 minutes after which 10 cc. of venous blood are withdrawn into a tube containing either citrate or oxalate crystals. A portion of this blood is then immediately placed in a Wintrobe sedimentation tube and the sedimentation rate

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determined. The remaining portion of the blood is adequately aerated until it is bright red, by rotation at 2-minute intervals for 15 minutes in an Erlenmeyer flask, after which its sedimentation rate is determined. The diagnostic parameter  $\Delta_2$  is indicative of sickle cell anaemia when the difference between the sedimentation rates (uncorrected) is greater than 20 mm. per hour. If the difference is less than 20 mm. per hour the chances are 10 000 to 1 against sickle cell anaemia and if the difference is greater than 20 mm. per hour the chances are 63 to 100 that the patient has sickle cell anaemia.

In the first method 5 to 10 cc. of venous blood are withdrawn into a tube containing citrate or oxalate crystals. A few cc. of this blood are then transferred to a rubber-stoppered Erlenmeyer flask into which pure  $\text{CO}_2$  is introduced, and the flask is agitated at 2 minute intervals for 15 minutes or until the blood becomes dark blue. A few cc. of the original blood are similarly treated in an open flask and aerated for 15 minutes or until the blood becomes bright red. The sedimentation rates of the two samples are then compared immediately in a Wintrobe tube and a difference greater than 27 mm. per hour between the rates is indicative of sickle cell anaemia.

In the study of 175 control patients with various diseases, including many types of anaemia, the average  $\Delta_2$  parameter was 5.3 mm. per hour the extremes being 1 and 18 mm. while the average for 34 patients with sickle cell anaemia was 41.4 mm. the extremes being 29 and 63 mm. per hour. The average  $\Delta_2$  parameter for 437 control patients was 3.5 mm. per hour. The extremes being 0 and 24 mm. per hour while the average for 73 patients with sickle cell anaemia was 53.5 mm. the extremes being 29 and 77 mm. per hour. Neither method gave a single false response. Sicklaemia that is the sickle cell trait without anaemia was not included in the series. A high concentration of  $\text{CO}_2$  is necessary for a satisfactory result and the gas used to saturate the blood with  $\text{CO}_2$  in the second method should contain not less than 85 per cent.  $\text{CO}_2$ .

Experiments showed that the more severe the anaemia the greater was the tendency for the parameter to deviate from the normal. Significant differences in the haematocrit determinations of bloods treated with  $\text{CO}_2$  and air occurred in patients with sickle cell anaemia. The increase in the haematocrit readings of patients suffering from sickle cell anaemia averaged 50.4 per cent. the extremes being 40 to 70 per cent following treatment with  $\text{CO}_2$ , whereas in control patients the increase averaged 10.9 per cent only with extremes of 4.3 and 21.4 per cent. Unless the effect of  $\text{CO}_2$  on the haematocrit reading is taken into consideration, grave errors may arise in the determination of the an corpuscular volume and the mean corpuscular haemoglobin concentration in haematological studies of patients suffering from sickle cell anaemia, as careless collecting of blood may involve venous stasis.

F. Alvingqvist

# VENOMS AND ANTIVENENES.

ROY NAV MED BULL. 1945 No. 17 40-46 3 pls. (1 folding) Poisonous Snakes.

This is a concentrated account in simple language of the systematic position, habits and venoms of poisonous snakes of the world. Some of the statements made might be challenged, but on the whole the information supplied is not highly inaccurate. It is incorrect to state that Many (vipera) have a dark inverted Y on the back of the head. Again, the general statement that venom is "ejected through a canal in the fang" refers only to the Viperidae there is no mention of the grooved fangs of the Elapidae. Sound advice is

given on first-aid treatment of snake bite with the exception of the recommendation that suction by the mouth should be carried out. There are several misprints in the table. For instance the tiger snake is *Notechis scutatus* the copperhead is *Denisonia superba* the moccasin is *Ancistrodon piscivorus* the spitting African cobra is *Naja nigricollis*. The statement in the table that *Naja nigricollis* is not very common is incorrect it is of course one of the commonest poisonous snakes in West Africa. The drawings accompanying this article would have been better omitted.

B G Macgrath

FREEDBERG A S & RISEMAN J E F Cobra Venom in the Treatment of Angina Pectoris. *New England J of Med* 1945 Oct 18 v 233 No 16 462-6 4 figs. [13 refs]

A contribution of the highest interest. Cobra venom has been tried for relief of pain in many conditions—cancer, tabes, leprosy, neuralgia and others—and benefit has been noted but always judged by the clinical history only, never objectively evaluated. It has been difficult to decide how much was due to the drug and how far the benefit was purely psychological because the use of inert placebos often gave relief. Among the cases on record in the literature are 14 of angina pectoris.

The authors' study is based on 12 cases of angina pectoris from coronary arteriosclerosis, existent for periods ranging from 2 months to 7 years. The amount of work necessary under standardized conditions to bring on the pain was gauged by RISEMAN and STERN's method, their standard exercise tolerance test. The patients were relegated to one of three groups. Group I reacting well to nitroglycerin and able under its influence to do double the work possible without the drug (4 patients). Group II able to do 50 per cent. more work after nitroglycerin (3). Group III giving no response to nitroglycerin or other usual methods of treatment (5). Seven out of the 12, four of them among the five of Group III, showed an improvement clinically and in standard exercise tolerance of the injection of cobra venom. The dosage at first was 1-2 cc. (10-20 mouse units, i.e. the m.l.d. for a 20 gm. mouse) daily injected into the deltoid for 3-7 days but the best dosage was found to be 1 cc. (10 mouse units) three times the first day then once daily for 7 days. The injections caused local pain but not severe enough to interrupt the course. Relief might last for some 5-6 weeks or for a few days only after the course was completed but the pain then returned and subsequent courses were less beneficial and although the treatment might be continued, the pain would return and the standardized exercise tolerance fall to the original level. No toxic effects followed from the dosage stated above but one patient who was given twice these doses on the first day suffered from pain in the chest, nausea, vomiting and diarrhoea of such severity as to call for cessation of the treatment. The important fact to be noted is that though the pain may be relieved the process underlying it—the pathological cause—remains unchanged and unaffected. The electrocardiogram after exercise is the same as that when no treatment is given. In other words the action of the venom is not to cause dilatation of the coronary vessels. Also as it takes some time—three days on an average—to bring about its effects the venom would be useless for relief of an acute attack.

[The action in relieving pain without affecting the underlying pathological condition is closely analogous to relief of pain by hypnotic suggestion. The abstracter knows of the case of a man suffering from angina pectoris applying to a medically qualified hypnotist for relief. The latter refused, stating that the pain which till then had not been very severe and was controlled by amyl

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nitrite was a warning to him not to hurry or over-exert himself. The patient applied to another hypnotist, not a medical man who gave him relief and he found he could do more such as quickening his pace to catch his morning train without pain. Soon after he hurried thus a little more than usual and died of a heart attack on getting into the railway carriage. The pain had been relieved, but the underlying condition remained, of course unaffected. This does not imply that the venom merely acts psychologically for cobra venom is known to be an analgesic.]

H Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES.

PETERS J T A Clinical Cure of Madura Foot. Amer J Trop Med 1945  
July 1 25 No. 4 363-5 2 figs (10 refs.)

Madura foot may be caused by any one of 13 species of *Actinomyces* or by any one of 19 species of true fungi (belonging to two classes and eight genera) yet the clinical picture is very similar in all cases this suggests that there is some common denominator. In the U.S.A. the usual cause is a true fungus *Monosporium apiospermum* cases due to *Actinomyces* being much rarer. The present case is probably only the third case of Madura foot due to *Actinomyces* in the U.S.A. that has been confirmed by culture of the organism. The patient a coloured man aged 53 was admitted to the Charity Hospital New Orleans on January 3rd, 1944 with a swollen left foot in which he said he felt occasional moderate pain. The swelling began in 1942, grew larger and discharging sinuses appeared. X-rays showed decalcification of the bones with small punched-out areas at the bases of the 3rd and 4th metatarsals and at the distal end of the 4th metatarsal. What appeared to be *Actinomyces asteroides* (Eppinger-Gasperini) was isolated from the pus of the sinuses.

Treatment.—Penicillin was given for four weeks without effect the total dosage being 1 050 000 units. Sodium propionate was next tried, as dressings containing 20 per cent and Iodides were not tried since they have always failed in Madura foot due to *Actinomyces*. Finally sulphadiazine 1 gm. every four hours in the daytime was given for three weeks the urine being always daily and the blood twice a week. The blood levels during the day were always about 8 mgm. per cent. His slight fever disappeared after one week of this treatment. A culture of slow growth was obtained at the end of the three weeks course but the patient refused further treatment as the swelling had much decreased in size and went home. He was advised to take methylsulphadiazine at home but did not do so for reasons of expense and for the same reason did not reappear for six months. His foot was then of normal size the sinuses had all healed, and he was able to do all his work as a farm labourer. He was again seen after six months and was still apparently quite well. The author regards the case as a clinical cure.

J F Corson

CARRIÓN A. L. & KNOTT J Mycetoma by *Monosporium apiospermum* in St. Croix, Virgin Islands. Puerio Rico J Pub Health & Trop Med 1944  
Sept. 1 20 No. 1 84-99 22 figs. on 7 pls [Refs. in footnotes.] [Spanish version 100-107.]

\* The first recognized case of madurumycosis in the Island of St. Croix Virgin Islands is herein studied and reported. The infection was of the white

grain type and its etiologic agent was a Hyphomycete identified as *Monosporium apiospermum* Saccardo 1911. Attention is called to certain morphologic peculiarities of this species which should be taken into consideration for future classifications.

CATANEI A & KERVRAN P. Nouvelle mycose humaine observée au Soudan français [A New Mycosis of Man found in French Soudan] *Arch Inst Pasteur d'Algérie* 1945 Sept v 23 No 3 169-72

The authors identified a case of histoplasmosis of an unusual type at Bamako in the French Sudan. The disease seems to have been localized in the right temporo-maxillary region where it formed a suppurating granulomatous tumor about the size of a hen's egg attached to the ascending ramus of the mandible. An exploratory puncture released about 20 cc. of brownish yellow fluid pus containing the fungus in the form of thick walled oval or rounded bodies having a longer diameter of 6-12 or even 15 microns some of which had an appearance of budding. In culture the fungus developed the characteristic morphology of *Histoplasma capsulatum* in the mycelial form. Reference is not made to the development of the yeast form in culture. The lesion was cured by injecting 1 cc. of lipiodol on two occasions into the cavity left after evacuation of the pus. The culture was infective apparently with little pathogenicity for mice and guinea pigs but not for rabbits. In the pus of the artificially induced lesions the fungus was found chiefly in the form of small yeasts 3-5 to 4-0 microns in diameter with occasionally a larger form.

[The question whether the *Histoplasma* isolated from African cases of histoplasmosis is a different species from *H. capsulatum* Darling 1906 is worth considering.] J T Duncan

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## HEAT STROKE AND ALLIED CONDITIONS

FARINAUD M E. L'homme et le climat colonial [The Influence of Tropical Climates on Man.] *Méd Trop* Marseilles 1944 May-June-July-Aug v 4 No 3 194-224 1 folding chart

In this review of the effects of tropical climates on man the author has gathered his widely ranging material under two main headings namely the Physical Climatic Complex and the Effect of Tropical Conditions on Organic Functions. The first includes the geographical and meteorological considerations required to explain tropical climatic characteristics and concludes with a series of climatograms for various areas in French Africa and Indo-China. These are built up on plots of mean monthly temperatures against mean monthly relative humidities at the different places. It is shown that the climatograms for most of the French possessions differ markedly from that of a typically temperate region inhabited by a white population and both are removed from the zone of maximum comfort.

In the second part of the review the author attempts to indicate how far the human physiological constants of temperate regions are altered by tropical conditions. Changes in the blood pressure and the concentration and composition of blood in basal metabolic rate and in excretory activity of skin and kidney are briefly discussed, but unfortunately where investigators are named no references are given to their publications.

The conclusion reached is that climatic conditions alone may cause a transitory effect but that so far they have not been shown to have any profound or lasting effect on the physiological functions discussed. This conclusion is also

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applicable to the psychological state of the inhabitant of the tropics. The author observes that the inconveniences and annoyances of colonial life often aggravated by excessive taking of alcohol or drugs form the groundwork on which the neuroasthenic and depressive states develop. He also stresses that the effect of the tropics on man can more adequately be considered as a meteoropathological problem, since many of the harmful effects imputed directly to the climate are often the result of pathological changes due to parasitic infections.

A. F. Blawie.

RIMERSCHMID Gertrud. Some Aspects on the Effect of Solar Radiation and other Factors of the Climatic Environment on Human Being. B Solar Radiation in South Africa and Europe and its Effect on the Human Body. C. The Ultra-Violet Solar Radiation. D The Interrelationship between Quantity and Quality of the Ultra Violet Solar Radiation and its Biological Effects. *South African Med J* 1945 Aug 25 Sept. 8 & 22, v 19 Nov. 16 17 & 18 282-5 308-10 331-4 19 figs. [27 refs.]

(An abstract of the first paper (Part A) was published in this Bulletin 1945, v 42 317.) Part B in this series of papers on the biological effects of solar radiation on man is concerned with the heating effects of visible and infra-red radiation. Part C deals with the intensity and quality of ultra violet radiation, and part D refers to the interrelationship between quantity and quality of solar radiation and biological effects. The data discussed came mostly from the South African Solar Radiation Survey of the Public Health Department. The intensities at different times of the day and at different seasons are compared with European observations.

The main factors influencing the total amount of radiation received on a surface is the inclination of the surface and the altitude of the sun, the length of day and degree of cloudiness. Radiation intensity is increased by altitude above sea level. In summer solar radiation is about the same in South Africa as in Europe but is much less in winter. A calculation is given showing that a 10-minute sunbath in South Africa is accompanied by the absorption of 60-70 Calories.

The chief effect of ultra-red radiation is immediate heat erythema accompanied by blistering if there is over-exposure to the far infra red rays. A calculation is given showing that a 10-minute sunbath in South Africa is accompanied by the absorption of 60-70 Calories. The chief effect of ultra-red radiation is immediate heat erythema accompanied by blistering if there is over-exposure to the far infra red rays. A calculation is given showing that a 10-minute sunbath in South Africa is accompanied by the absorption of 60-70 Calories.

It is concluded that the large amount of solar radiation reaching the earth's surface in South Africa must have physiological and psychological effects on its population.

The intensity of ultra violet radiation is determined by the ozone content of the atmosphere, the turbidity of the air and the thickness of the atmospheric haze. Sky radiation contributes as much as direct solar radiation. The total amount of ultra violet radiation is 5-10 times greater in South Africa than in Europe. There is also a greater proportion of shorter wavelength radiation. The intensity of the lower ultra violet wavelengths is much smaller when the sun is nearer the horizon.

Ultra violet radiation produces several specific effects due to its actinic action. This action is mainly restricted to wavelengths shorter than 330 mμ. The "relative effectiveness" of a particular wavelength is a function of the biological effectiveness relative to the intensity of radiation at that wavelength. Curves are given showing the relative effectiveness for three different biological effects viz. erythema, bactericidal action and ergosterol transformation. There is a notable increase in effectiveness with higher sun altitude.

The erythema effect would appear to aggravate the skin lesions in chicken pox. This may be important in regard to other infectious diseases in the tropics.

If ergosterol behaves in the human skin as it does *in vitro* a certain antirachitic effect can be expected even if the sun only rises to  $15^{\circ}$  as in Northern Europe in winter. South Africa obtains considerably more of this ergosterol transforming ultra violet radiation but whether there is too much of it in South Africa's sunshine will not be known until some idea has been formed as to the amount of natural radiation essential to produce an adequate vitamin D supply for adults.

A F Munro

WEINER J S The Regional Distribution of Sweating J Physiology 1945  
June 29 v 104 No 1 32-40

This paper describes an attempt to partition sweat loss in three male subjects according to anatomical region. The men were in process of acclimatization to an effective temperature of  $94^{\circ}\text{F}$ . Profuse sweating was induced by continuous step-climbing during the first two hours of exposure the effort being sufficient to raise the rectal temperature to slightly over  $102^{\circ}\text{F}$ . Observations were made during 50-60 minutes following the last work period, when rectal temperature was maximal.

Sweat was collected from a number of small areas on the head, trunk, thighs, legs, feet, arms and hands. Collection was made from three successive groups of ten areas each group including areas from every region in order to reflect at each stage the rate of sweating from the body as a whole. The technique involved initial drying of the skin in the area selected followed immediately by application of a metal ring 7 cm. in diameter and 2 cm. in depth. A well fitting lid prevented loss of sweat. The sweat samples were collected over periods of  $2\frac{1}{2}$  minutes during the last 30 seconds of which they were mopped up on previously weighed cotton pledgets.

The difference between the observed overall sweat loss and the combined sweat loss calculated from the regional losses did not exceed  $\pm 8$  per cent. The general conclusions drawn from the experiments are as follows —

- (1) There are marked variations in the rates of sweating in different areas of each anatomical region, but approximately 60 per cent of the sweat is lost from the trunk, 25 per cent. from the lower limbs and 25 per cent from the head and upper limbs.
- (2) The rate of sweating is greater about the 8th day of acclimatization to heat than on the 3rd day.
- (3) The relative intensity of sweating is calculated by dividing the proportion of total sweating contributed by a region by the proportion of total surface represented by that region. The relative intensity is greatest on the trunk and next greatest on the head and varies on other areas according to the individual. Sweating is least on the hands which are affected more by mental than thermal stimuli.

The author discusses how far these differences may be related to number, size or activity of the sweat glands. In the absence of experimental evidence he suggests that in some areas e.g. the trunk there may be a greater reserve of unused glands or that individual glands may be on the average larger. The author might have made the meaning of the term 'relative intensity' clearer by stating that it is calculated by dividing the rate of sweating per unit area of a particular region by the mean overall sweating rate per unit area of the body.]

A F Munro



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LADELL, W. S. S. The Effect of Desoxycorticosterone Acetate on the Chloride Content of the Sweat. *J Physiol* 1945 June 29 v 104 No. 1 Proc. Physiol. Soc. 13P-14P

"Daily intramuscular injections of 10-15 mg of desoxycorticosterone acetate (DOCA) in man increase body weight and plasma volume and reduce sodium and chloride excretion without changing serum sodium and chloride." Diminished urinary sodium and chloride may be the result of a direct action on the kidney tubules. The author here shows that DOCA has an action on the sweat glands, and by collecting sweat and estimating its chloride in subjects working in a hot room before and during a course of injections of DOCA (10 mgm. doses) found that about 30 per cent less salt was lost in the sweat during the course than before it. The subjects of the experiment gained weight and became oedematous but the effect passed off 72 hours after the last injection.

Charles W. Loocks

### TROPICAL ULCER.

VINCENT Hyacinthe. Remarques sur l'étiologie la pathogénie et l'agent pathogène "*Bacillus fusiformis*," de l'ulcère phagédénique. [The Aetiology Pathogeny and Pathogenic Agent, *Bacillus fusiformis* of Phagedenic Ulcer? *Bull Acad Med* 1945 v 129 No. 30 31 & 32, 545-8]

The author was surprised to read in a recent paper by BALOSET DURAND and RAGU (*Bull Acad Med* 1945 v 129 533) that there are two types of *Bacillus fusiformis* the non-motile type of Vincent and the motile type of Plant. Both motile and non-motile forms were described by Vincent, who found them together in the same microscopic field as for Plant's bacilli, the latter observed "Miller's bacilli," which were really *Spirillum putigenum* and from *Spirochaeta vincentii*.

Phagedenic ulcer according to the author is caused by *B. fusiformis* frequently in association with *Sp. vincentii* and other micro-organisms especially staphylococci, and streptococci. When material from an ulcer was injected into the healthy tissues of healthy guinea-pigs and rabbits, no ulcer was produced, but when the injection was made into the previously crushed tissues of these animals which had been kept on a low diet for a few days and especially when other organisms—staphylococci or *Pseudomonas*—were also injected at the same time typical ulcers were produced. In the tropics ulcers occur in persons who are debilitated by such causes as malnutrition excessive fatigue, or some other infection some races are more susceptible to the infection than others.

The author has successfully treated phagedenic ulcer by first cleaning it with normal saline then drying it and applying a mixture of dry powdered calcium hypochlorite 1 part and dry boric acid powder 9 parts the dressing was renewed every 3 or 4 days. The surrounding skin was painted with tincture of iodine. A suitable diet was prescribed. Healing usually took place in 2 or 3 weeks.

F. Corson

MORANTY J. K. So-called Tropical Ulcer in Angul. *J Indian Med Ass* 1945 Aug., v 14 No. 11 263-6 & 262, 1 graph & 1 fig. [17 refs]

The occurrence of tropical ulcer in Angul, India, had not been reported before 1942, but in that year and the following one many cases occurred the

infection appeared to have been introduced from Assam by returning soldiers [see also this *Bulletin* 1944 v 41 614 *ibid* 1945 v 42 405] Poverty stricken badly nourished people nearly all men, were chiefly affected.

Smears taken from the ulcers showed abundant diphtheroid bacilli in 4 cases *Bacillus fusiformis* was present without diphtheroids. No facilities for culture were available but several experiments were done on the patients and on pigeons. Ulcer discharge fluid containing diphtheroids was injected intradermally and produced typical ulceration in 7-8 days and the same result was obtained by injecting conjunctival discharge containing diphtheroids if the material injected was previously heated no ulcers were produced. The injection of diphtheroid-containing material into the chest muscles of pigeons caused inflammation and fever and the birds died in 2-5 days.

No immunity apparently developed other ulcers occurred even during convalescence

The leg and the dorsum of the foot were chiefly affected in a few cases the ulcer was on the elbow forearm or thigh but none was seen on the sole or on the face Regional lymphatic glands were not involved. No peripheral neuritis was observed.

*Treatment*—Many applications were tried but none seemed better than another a simple daily dressing with complete rest of the limb was beneficial The injection of 4 000 units of antidiphtheritic serum daily for 3 days had no apparent effect on the ulcers  
J F Corson

SESHADRINATHAN N Tropical Ulcer A Study of One Hundred Cases collected in the City of Madras. *Indian Med Gaz* 1945 July v 80 No 7 344-6.

The author made observations on 100 cases of tropical ulcer in the city of Madras The size of the ulcers varied from  $\frac{1}{2}$  in to 2 $\frac{1}{2}$  ins in diameter 73 out of 84 not exceeding 1 in. of 95 ulcers 62 were on the foot 32 on the leg and 1 on the elbow The ulcers were painful and very tender The ages of the patients ranged from 7 years to over 50 years Thirty were weavers by trade and only 4 of these gave a history of trauma as a cause of the ulcer whereas half of the others gave such a history The weavers work with their legs in long pits in which the handlooms are lodged the pits are warm and moist and lined with cow-dung but it is not known whether insects took shelter in the pits Persons of the class of the patients drink little or no milk.

Spirochaetes and fusiform bacilli were present in the ulcers the longer forms of the fusiform bacilli being motile pure cultures of fusiform bacilli were grown on 1 per cent. agar containing 25 per cent. of rabbit blood incubated at 37°C. in an atmosphere of 90 per cent. of hydrogen and 10 per cent. of carbon dioxide but subcultures could not be maintained.

In treatment the best results were obtained with gauze soaked in a warm 5 per cent. solution of copper sulphate.  
J F Corson

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## MISCELLANEOUS DISEASES

OGILVIE W H Pitfalls of Tropical Surgery *Lancet* 1945 Nov 10 585-7

The author was a consulting surgeon to the East Africa Force in 1940-42 and to the Middle East Force in 1942-44 and discusses some of the puzzling aspects of surgery which he encountered in Africa he selects as subjects three diseases—amoebiasis malaria, and bilharziasis—and the peculiarities of the African as a patient

Amoebiasis is generally seen by the surgeon in a chronic stage in two patients an amoebic abscess of the liver simulated gall-stones and two cases of intussusception beginning at an amoebic mass in the caecum were seen, while an amoebic mass in the rectum was mistaken for a carcinoma and a left inguinal colostomy was performed. The author suggests that toxic absorption from the ulcerated bowel may cause subacute arthritis of the synovial type. Operation for haemorrhoids, fistula or anal fissure should not be done within two months after the end of an attack of dysentery and not without preliminary sigmoidoscopy.

Malaria complicates surgical diagnosis and disturbs treatment post operative and post traumatic rises of temperature are almost universal in malarial countries. In abdominal conditions particularly diagnosis is made more difficult.

Bilharziasis was probably responsible for failure to catheterize the ureters on many occasions several instances of bilateral dilation of the ureters were seen in South African officers.

The African appears to be a biological species distinct from Northern man the author notes his freedom from arterial disease duodenal ulcer and parasymphilia even when he adopts town life. The African suffers from acute arthritis and bone disease which appear to be due either to syphilis or yaws. Primary carcinoma of the liver is common among the Bantu races. The author concludes with the sentence But the standard textbook on tropical surgery has yet to be written.

J F Corson

WILLSON PEPPER, J. K. Impressions of Surgery in West Africa. *Brit Med J* 1945 Dec. 8, 812-14

The author was a surgeon at a hospital in a swampy mosquito-infested region of West Africa for 18 months his patients were nearly all European troops and he found unexpected differences in the course of surgical diseases and the effect of treatment from what he had previously experienced in temperate climates staphylococcal infections for example being particularly severe. In this paper he records his general impressions received during that period of work in tropical Africa.

J F Corson

CROPPER, C. F. J. Amoebiasis. [Correspondence.] *Brit Med J* 1946 Feb 2, 181

The author disagrees with the opinion of WILLSON PEPPER [above] that the proctoscope may be used instead of the sigmoidoscope with equal results for the diagnosis of amoebic dysentery in his experience the only visible lesions in a very large percentage of cases are at 5 to 6 in. from the anal margin. He agrees that exhausting wash-outs should not be given before the rectal examination but considers that two or three weak soap or bicarbonate enemas may be given three hours before the examination [with the sigmoidoscope] with advantage.

J F Corson

VISWANATHAN R. Pulmonary Eosinophilosis. *Indian Med Gaz.* 1945 Aug v 80 No 8 392-8. [11 refs.]

The condition here dealt with has several synonyms pseudo-tuberculosis with eosinophilia, benign eosinophilic leukaemia, tropical eosinophilia, eosinophil lung, and the author now suggests another a variant of the last namely pulmonary eosinophilosis. He gives a brief review of 85 cases seen during a period of 14 months among nearly 1 000 admissions to hospital for respiratory

troubles. Though they originally came from different Provinces all had been in East Bengal or Assam recently for 3 months or more so a humid climate may play some part in the aetiology. The chief symptom was troublesome but unproductive cough with fever in 51 (60 per cent.) and sometimes asthma like attacks. Physical signs were few basal râles and slight tachycardia, and rhonchi in the asthmatic. Eosinophiles constituted 15 to 80 per cent. of a total leucocyte count of 10 000 to 50 000. X rays showed small dissomiated shadows but these are seen in the acute phase only and their absence does not exclude the diagnosis. The blood often gave positive cold agglutination of pneumococci as in some cases of atypical pneumonia. Occasionally there were unusual features such as widespread lymphadenitis pleurisy with effusion palpitation and precordial pain. Arsenicals bring about a speedy cure though the first injections increase the eosinophilia. The usual method is an initial dose of 0.15 gm. NAB and twice this every 5 days after till symptoms disappear.

As regards causation the author considers previous suggestions of mites (as found by CARTER WEDD and D ABRERA see this *Bulletin* 1945 v 42, 73) he looked for them without success in 6 of his cases atypical pneumonia (because of the high titre cold agglutination test) and the inevitable virus.

H Harold Scott

FAHIS R. A. Eosinophilic Infiltration of the Lung (Report on Two Cases) *J Palestine Arab Med Ass* 1945 Nov v 1 No 1 17-20

BENT M J TURNER, E. L. HOLLOWAY G D & CUFF J R. Nutritional Deficiency as an Etiological Factor in Icterus accompanying Pneumonia in the Negro. II. Value of Brewer's Yeast in preventing Icterus in Pneumonia. *Southern Med J* 1945 Nov v 38 No 11 730-33 [12 refs.]

From clinical evidence and experiments on dogs the authors [this *Bulletin* 1944 v 41 148] concluded that a high incidence of jaundice in a group of adult negroes was due to a badly balanced diet associated with poor cooking. In the present paper experiments to test the protective action of the vitamin B complex when added to the same deficient diet as was used in the previous experiments are recorded.

Nine dogs (controls) were placed on the restricted diet only and 11 other dogs were given the same diet with the addition of brewer's yeast. After the dogs had been on the diets for 21-49 days pneumonia was induced by the insufflation of pneumococci (Type 1 Robertson strain). Van den Bergh tests were made daily before the insufflation and twice daily afterwards. The dogs were killed and examined one to four days after the insufflation.

None of the 11 dogs on the diet plus yeast developed a positive van den Bergh reaction while all the 9 controls did. All the control dogs lost weight while none of the others did, and 5 of them gained weight the former however rejected more and more of their food as time went on.

Post mortem examination showed that all the 9 controls had pneumonia and extensive fatty changes in the liver the other 11 dogs had less severe pneumonia, 5 of them showed no pathological changes in the liver and only one showed changes comparable with those observed in the controls.

The results support the conclusions reached in the previous observations and experiments.

J F Corson

DESPUJOLS B BERGERET C CALMIET L. & ROUVIER J. Sur un cas de mélioidose à évolution prolongée. [A Case of Melioidosis with Prolonged Course.] *Alld Trop* Marseille. 1942, Nov v 2, No 9 689-702. [10 refs.]

## GENERAL PROTOZOOLOGY

KIRBY H. The Structure of the Common Intestinal Trichomonad of Man. *J Parasitology* 1945 June v 31 No. 3 163-75 27 figs. on 3 pls. [18 refs.]

The author has studied cultures of two strains of trichomonads of the human intestine employing dark-field illumination and films fixed in Hollande's cupric picroformal and impregnated with silver by activated protargol as recommended by BODIAN for nervous tissues and adapted to protozoological technique by COLE and DAY. By the impregnation technique a flattened structure not hitherto described was found at the anterior end of the body. It is termed the pelta. It lies to the right of the blepharoplast-complex and is continued as a filament in the cytoplasm dorsal to the nucleus. A small ellipsoidal parabasal body lying against the anterolateral surface of the nucleus was also demonstrated. In other respects the findings are mainly in agreement with those of WEXLER: this *Bulletin* 1944 v 41 687-698 particularly with regard to the existence of five anterior flagella four of which, directed forwards have a common origin in the blepharoplast-complex, while the fifth originates independently from this complex and is directed laterally or posteriorly. The author follows WEXLER "in his opinion that there is one species that is commonly found in the intestine of man and, in fact, there are grounds for surmising that there is a possibility, that all accounts of trichomonads from that situation, except that of *Tritrichomonas faecalis* have actually dealt with the one species." The author considers that the presence of 5 flagella one of which arises independently of the others justifies the use of the generic name *Pentatrichomonas* the intestinal trichomonad of man being denominated *Pentatrichomonas hominis* (Davame 1860). The paper is illustrated by a series of drawings and microphotographs showing the various structures revealed by the technique employed. C. M. Pennyon.

TRUSSELL, R. E. & JOHNSON, C. *Trichomonas vaginalis* Donné. Recent Experimental Advances. *Puerto Rico J. Pub. Health & Trop. Med.* 1945 Mar v 20 No. 3 239-505 8 figs. on 2 pls. Refs. in footnotes. Spanish version 306-21.

CALLAHAN, W. P. Jr. The Incidence of Toxoplasmic Infections in the St. Louis Area. *Proc. Soc. Exper. Biol. & Med.* 1945 May v 59 No. 1 68-70.

As cases of toxoplasmosis seemed to be of fairly frequent occurrence in the St. Louis area of U.S.A. the author decided to test sera from apparently healthy individuals by Saben's neutralization method, in which varying dilutions of serum mixed with toxoplasmas are inoculated into the skin of rabbits. Eight fatal cases of toxoplasmosis had been observed in St. Louis since 1940. Two were in adults who suffered from an acute febrile condition associated with a skin rash, resembling the typhus-spotted-fever group of diseases. The other cases were in infants in whom the disease was apparent at birth or commenced soon after. There was widespread involvement of the central nervous system giving rise to generalized convulsions, muscular paralysis and internal hydrocephalus. Cerebral calcification and encephalomyelitis with the formation of many granulomatous lesions were the chief pathological changes. Toxoplasms were present in small aggregates or in pseudocysts and as free organisms in the central nervous system. Of 100 sera tested, 74 were from inhabitants of St. Louis and 26 from persons outside the state of Missouri. Only two of these sera prevented the production of skin necrosis by the toxoplasma injected.

These were from unmarried girls 18 and 21 years of age of the St. Louis area. Neither showed any evidence of present or past illness which might be interpreted as toxoplasmosis  
C M Wenyon

WEINMAN D La toxoplasmosis en el hombre [Toxoplasmosis in Man.] *Dis Médico* 1945 Oct 8 v 17 No 41 1164-70 2 figs.

## GENERAL ENTOMOLOGY

HADDOW A J The Mosquitoes of Bwamba County, Uganda. III. The Vertical Distribution of Mosquitoes in a Banana Plantation and the Biting Cycle of *Aedes (Stegomyia) simpsoni* Theo *Bull Entom Res* 1945 Nov v 36 Pt 3 287-304 3 figs

The vegetation and climate of the Bwamba area were described in Part I and the activity of the local mosquitoes was dealt with in Part II of this series of papers [see this *Bulletin* 1946 v 43 79 80] The third part is mainly concerned with the biting activities of *Aedes simpsoni* (the vector of human yellow fever in Bwamba) at different vertical levels

Four catching stations were established near a large banana plantation. One was on the ground among heavy undergrowth, the other three were on platforms in the trees. The first of these was erected at six feet from the ground among leaves of young plants, the next was at 12 feet among leaves of full-grown plants, and the highest was at 18 feet in the open air above the tallest plants.

The catching of mosquitoes from human bairs at all four stations was done simultaneously and continuously for ten days, five of which were hot and bright with cold mornings, and the other five warm and cloudy with warm mornings. Catches for each hour from each level were recorded separately.

The total catch was 687 mosquitoes belonging to 16 species (counting the mixed *Culex* spp. as one). The vertical distribution of all species was as follows: 210 (eleven species) at ground level, 182 (nine species) at 6 ft, 167 (seven species) at 12 ft, and 128 (six species) at 18 ft. *Aedes simpsoni* accounted for 596 of these as follows: 179, 159, 141 and 117 at the respective levels. Other species were so scarce that their numbers were inadequate for discussion, but it is noted that sylvan species such as *Anopheles implexus* (1), *Aedes apicoargenteus* (1) and *Aedes africanus* (3) were present in the catches though the nearest breeding places of *Aedes apicoargenteus* and *Aedes africanus* were in the forest half a mile away where larvae were abundant in tree holes.

By grouping the catches in hourly and four hourly periods, it is shown that *Aedes simpsoni* is a strictly diurnal species, most active on the warm, cloudy days which produced 445 as against 151 for the hot, bright days with cold mornings.

The principal raiding monkey in Bwamba is *Cercopithecus mitis* *mpangas* Matschie, the common red tail or white-nosed guenon. Out of 41 of these monkeys, 25 were found to be immune to yellow fever, and it is suggested that an infected monkey feeding on the bananas at the 12 ft. level could easily pass on the yellow fever virus to *Aedes simpsoni*.  
H S Leeson

ADAM N K A Rapid Field Method for assessing the Spreading Power of Anti-Malarial Oils. *Bull Entom Res* 1945 Nov v 36 Pt 3 269-72.

It is essential that an oil used for killing mosquito larvae should spread completely over the surface of the water to be treated. Most natural waters

especially if stagnant, are already covered with a film, either visible or invisible which the spreading oil must push aside. The efficiency of the antimosquito oil therefore, depends to a large extent on its spreading pressure. In the laboratory this can be measured directly in dynes per centimetre (see ADAM *Proc Roy Soc B* 1937 v 122, 134) but it is often important to use a more simple method, and portable apparatus especially in the field.

The method suggested employs a prepared series of liquids of standard spreading pressure. These are either compared with an unknown liquid on a clean surface, or tested against a natural film the substance producing a film with the greater pressure will push back the other film. In the laboratory rapid tests are made with a large glass funnel cleaned and kept clean by water overflowing round the rim from a supply through the stem. The water flow is stopped and a little water tipped out to lower the level just below the rim a drop of one oil is applied to the surface covering it with a film and leaving a lens of about a quarter of an inch in diameter. The second liquid is then added and the effect observed. If necessary talc powder can be shaken on to facilitate observation of movements of the films.

The liquids of choice for the standards may be used alone or as solutions in non-spreading mineral oil (medicinal paraffin). They must not be volatile and they must not be affected by the pH range to be expected in natural waters. The following series are recommended —

#### Standard Spreading Liquids

	Spreading pressure dynes per cm. 20°C
Methyl or ethyl salicylate	13
Dimethyl or dibutyl phthalate	21
Terpineol, liquid (from B D H. Ltd.)	38
Oleyl alcohol (from I.C.I. Dyestuffs Ltd.)	47

#### Standard Spreading Solutions.

Solvent B.D.H. Liquid paraffin S.G. 0.835-0.850

Terpineol in paraffin		Oleyl Alcohol in paraffin	
cc. Terpineol per 100 cc. sol.	Sp. pressure dynes/cm. 20°C	gm. Oleyl Alcohol per 100 cc. sol.	Sp. pressure dynes/cm. 20°C.
0.1	4.5	0.2	13
0.2	7.5	0.5	17
0.5	13	1.0	25
1.0	18	2.0	30
2.0	21	5.0	37
5.0	25	10.0	48
10.0	30		

J. R. BURRINE

HOEHN, D. Nephrosis probably due to Excessive Use of Six-way Insect Repellent. *J. Amer. Med. Ass.* 1945 June 16 v 128 No. 7 513

A white boy aged 3 years was admitted to hospital on 4th August, 1944 acutely ill with generalized oedema. His urine contained pus and albumin but no casts. He improved for a few days then the oedema increased and by September he appeared to be dying. He was given four plasma infusions and two blood transfusions after which he gradually improved and at the time of writing was in fairly good health.

During the whole of the summer an insect repellent called Sta way had been freely applied to his skin tests were made on rabbits and it was found that Sta way was a strong kidney and liver poison

The author concluded that the child had suffered from nephrosis due to the application of Sta way  
J F Corson

Niño F L. & FERNANDEZ J C. Miasis cutánea por larvas de *Cochliomyia hominivorax* (Coquerel 1858) [Cutaneous Myiasis due to *C. hominivorax*] *Bol Inst Chm Quirurg* Buenos Aires. 1945 May v 21 No 173 281-6 8 figs.

STANBURY J B & HUYCK J H. Tick Paralysis a Critical Review *Medicine* 1945 Sept. v 24 No 3 219-42 [77 refs.]

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### LABORATORY PROCEDURES

MERTENS Elizabeth A Simple Technique of Sternal Marrow Biopsy for Spreads and Sections *Amer J Med Sci* 1945 Nov v 210 No 5 630-34 6 figs.

The author describes a method of sternal marrow aspiration which has most of the advantages of both the aspiration and the trephine methods without their disadvantages it resembles the aspiration method but differs in that the blood is allowed to clot and sections can therefore be made

The skin subcutaneous tissues and periosteum having been anaesthetized with 1 per cent. novocain solution a 15 gauge Osgood sternal puncture needle is entered in the mid-sternal line at the level of the upper border of the 3rd costal cartilage. The stylet is removed when the marrow cavity is reached and the needle is then gently pushed on at an angle of 90 to 40 degrees for not more than 7 mm. in an adult or until the resistance of the posterior lamella is felt. A dry 10 cc syringe is then attached and sternal marrow and blood are aspirated to a height of 2-3 mm. in the syringe The tip of the syringe should have a bore equal to that of the needle The syringe is detached and the plunger withdrawn for about 1 cm. and the contents allowed to clot when clotting is complete the plunger is withdrawn with the attached clot which is then put into fresh Zenker's formal solution for fixation Paraffin sections are cut and stained with Azure II Eosin.

To obtain films the needle is withdrawn as far as the anterior lamella the stylet removed and the needle passed again into the marrow cavity in a slightly different direction a second syringe is attached a second specimen aspirated the stylet reinserted and the needle removed.  
J F Corson

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### REPORTS SURVEYS AND MISCELLANEOUS PAPERS

Sicé A Role social du médecin colonial en Afrique Française [The Social Function of Colonial Medical Officers in French Africa.] *Méd Trop* Marseilles. 1944 May-June-July-Aug v 4 No 3 163-63

The French language is perhaps the most perfect medium for dignified and persuasive prose and General Sicé is a master of its use. His theme is worthy



situated on the outskirts of the town in the years 1938-1941 the average monthly numbers of patients treated were 850 1,950 3 020 and 3 700 and in the summer of 1941 over 5 000.

Kabul, an old town with a population of 140 000 has many narrow crooked, unpaved streets and houses built of mud. It has however a pipe borne water supply brought from the mountains about 20 miles away. The water is good and is periodically examined, and if an epidemic is threatened, it is chlorinated. The water supply is insufficient for modern needs and the new houses in the suburbs have water tanks which are filled daily. The drainage of surface and waste water is primitive but in the newer parts covered soakage pits in the dry porous soil are satisfactory. The latrines are simple pits.

Some years ago the lay-out of a new town was begun. It was originally planned as a university town with modern construction, sanitation and water supply.

The duties of the health officer include street cleaning supervision of markets slaughter houses and food bazaars bath houses and the drainage of waste water. In addition there are preventive measures against malaria, cholera, smallpox and trachoma, and efforts to obtain greater care of infants and small children. As in some other Mohammedan countries the seclusion of women is a hindrance to medical progress.

Modern Afghanistan strives to keep in touch with Western European science. A Review of Hygiene in the Persian language has been published for some years. In the author's time some Afghan students who had studied in Europe together with some French naturalists in Afghanistan, founded a society for the study of valuable products of the earth—minerals, medicinal plants and medicinal springs. This had the interest and support of the Ministers of Health and Agriculture.

The author describes briefly the chief infectious and non-infectious diseases of the country. *Malaria* benign tertian and subtertian, is widespread.

Iran malaria is unknown and there is no record of *blackwater fever*. Little known of anopheline vectors. *Kala azar* is not known to occur but cutaneous leishmaniasis is present and *Phlebotomus* abounds. It is unknown whether canine leishmaniasis exists in the country. *Trachoma* is very common. In Kabul it affects about 13 per cent of the population. *Relapsing fever* of the Persian type, probably tick-borne occurs in the spring and early summer. *Typhus* never in epidemic form is present from January to April, *typhoid* and *paratyphoid* A and B in the late summer autumn and first part of the winter. *Bacillary* and *amoebic dysentery* occur the latter being widespread though amoebic carriers were found among the Germans resident in Kabul, no amoebic dysentery is known there. *Shiga-Kruze Flexner* and *Sonne* types of dysentery bacilli *Salmonella breslau* and *Bact. fecalis alkalicus* have been isolated. Acute intestinal diseases cause a large part of the high mortality among small children. *Cholera* *smallpox* and *plague* occur sporadically. In 1938 an outbreak of cholera occurred, with 3,291 cases and 1 710 deaths. Nearly half a million persons were vaccinated and there was no outbreak in the following year. *Undulant fever* and *abortus fever* are not known to occur. *Leprosy* is present but its extent is unknown. It is estimated that there are from 1,200 to 3 000 cases in the whole country. It was proposed to form a leper settlement, largely self-supporting about 10 miles from Kabul but the war prevented the carrying out of the plan. Little is known of the prevalence of venereal disease. The author saw only a few cases of syphilis and gonorrhoea in Kabul. Few cases of *dysphtheria* and *scarlet fever* are seen, but *measles* is prevalent and ranks after *smallpox* and *whooping cough* as a fatal disease in children. *Tuberculosis* in Kabul appears to resemble the disease in Europe.

in its incidence and course extrapulmonary tuberculosis appears to be rather common. Various other cosmopolitan diseases occur and call for no special mention.

The author thinks that the high mountain ranges on the eastern side form an epidemiological barrier as well as a geographical one. In its epidemiology Afghanistan resembles the countries on the western side where there are few geographical barriers. The paper contains many references to medical reports of neighbouring countries.

J F Corson

NOTESTEIN F W & JURKAT E. Population Problems of Palestine. *Milbank Memorial Fund Quarterly* 1945 Oct v 23 No 4 307-52 18 figs

## BOOK REVIEWS

ACKERKNECHT E H. Malaria in the Upper Mississippi Valley 1760-1900. *Suppl to the Bull History of Med* 1945 No 4 pp viii + 142 with maps & figs [Bibliography]

The Upper Mississippi Valley is one of those interesting regions from which malaria once very prevalent disappeared long before the introduction of any systematic antimalarial measures and largely before the acquisition of knowledge of its mode of transmission. In this very interesting monograph the author has gathered together a surprisingly large amount of information from records of the early days of the conquest and settlement of the great continental heart of North America when ague was so formidable a menace to health along the rivers which constituted the chief means of communication. From then up to recent times the records have been searched for information bearing on this fascinating epidemiological problem and the search has been fruitful.

The five States included in this area Illinois Missouri Iowa Wisconsin and Minnesota are each described and considered independently. A map of each State is attached. Then the factors which may have contributed to the elimination of the scourge of malaria are discussed in turn and numerous authorities are quoted. The factors considered are population movements steamships railroads and river regulation clearing cultivation and drainage prosperity housing screening food education cattle breeding mosquitoes quinine climate. Clear and concise answers to the innumerable questions raised in inquiries of this nature are hardly to be expected but the author does show that the arrest of population movements was accompanied by a decline of malaria incidence in Missouri Iowa and Wisconsin. Another important factor was the shifting of settlements away from watercourses that resulted from the construction of railroads. Drainage enterprises may have speeded up the decline of malaria in Illinois but elsewhere the decline preceded organized drainage. Better housing and an increase in dairy cattle characterized the period of malaria decline. To quote the author's concluding words it may be well to remember that malaria in the Upper Mississippi Valley was not killed by a single magic bullet. The monster was only put in chains the links of which we have tried to study. Each link of the chain is important and the breaking of one link may set free again the evil fiend. But as the author repeatedly states the climate in the Valley is not very favourable for malaria.

Norman White

CASTILLO Roberto Levi. *Los anofelines de la Republica del Ecuador* Vol. 1 172 pp., numerous figs. maps & pla. 1945 Guayaquil Ecuador Artes Graficas Senefeldor C. A. Ltda.

This is a systematic and adequate description of the *Anopheles* hitherto recorded in the Republic of Ecuador. An introduction details the salient geographical features of the country and the climatic conditions. The equator traverses the north of Ecuador. The three natural geographical regions of the country are: a coastal region between the Pacific Ocean and the western escarpment of the Andes, comprising the provinces of Esmeraldas, Manabi, Guayas, Los Rios and El Oro; a mountainous Andes region comprising the provinces of Carchi, Imbabura, Pichincha, Cotacachi, Tungurahua, Chimborazo, Bolivar, Cañar, Azuay and Loja; and an eastern Amazon region wedged in between Colombia and Peru and the eastern escarpment of the Andes, and comprising the provinces of Napo-Pastaza and Santiago-Zamora. The species of *Anopheles* found in these three regions are: Western coastal region, 4 (*Chagasia*) *bathensis*, 1 *pseudopunctipennis leucostilloi*, 1 *crueni*, 1 *punctimaculata*, 1 *apicimaculata*, 1 *mediopunctatus*, 1 *albimanus*, 1 *aquasalis* and 1 *netoi*; Central Andes region, 1 *pseudopunctipennis rrodenburgi* and 1 *crueni*; Eastern Amazon region, 1 *bolivensis*.

All these species are fully described and illustrated. *A. albimanus* is the main vector of malaria throughout the coastal provinces where it is very widespread: infection rates of from 3 to 5 per cent. have been recorded. The author believes that Ecuador is the southern limit of distribution of *A. bathensis*: it has never been reported from Peru. Of the two races of *A. pseudopunctipennis* found in Ecuador *A. pseudopunctipennis rrodenburgi* is the chief vector of malaria in the warm highland valleys. It is found in all the provinces of the central Andes region and has been found as high as 2,500 metres. It has a marked preference for human blood. In contrast *A. pseudopunctipennis leucostilloi* exhibits marked zoophilism: it is not found at altitudes above 300 metres. *A. crueni* is a wild species and is zoophilic: it has been found at altitudes ranging from 88 to 2,100 metres. *A. apicimaculata* was found in five of the central Andes provinces: it is zoophilic and is only met in jungle far from human habitations. *A. mediopunctatus* occurs in coastal jungles but is very rare. *A. aquasalis* is the only species found breeding in brackish water in Ecuador: it breeds in crab holes in banks of inlets from the sea in the coastal provinces. *A. (Kertessia) netoi* breeds exclusively in bromeliads in the five coastal provinces. *A. (Kertessia) bolivensis* of similar breeding habits is very abundant in the Amazon provinces of Ecuador. It frequents human dwellings and has a preference for human blood: it is a suspected vector of malaria.

The numerous photographs appended to this small volume are very indifferent and add nothing to its value.

Norman White

FINNEMAN Susan [B.Sc. Ph.D.] *Acarid as Agents transmitting Typhus in India, Australasia and the Far East. British Museum (Natural History) Economic Ser. No. 16* 78 pp., 49 figs. (2 maps 1 folding) 1945 London. Printed by Order of the Trustees of the British Museum. [1s. 6d.]

The serious military problem presented by scrub typhus in S.E. Asia and the S.W. Pacific during the war was generally quite unexpected. Few people had any practical experience of the disease and a great demand for information and literature therefore arose. Dr Susan Finnegan's book is intended to make modern knowledge about the vectors of scrub typhus, and of other rickettsial diseases transmitted by mites and ticks, easily accessible to workers in the

field. This sort of information is otherwise almost entirely inaccessible to such workers and the book should be widely welcomed. Clear diagrams and useful keys make identification of the important species possible.

From the strictly entomological point of view the greater part of the contents of this book will probably require little in the way of fundamental modification in the near future though additional sections may be required. But since it went to press there have been many papers dealing with the transmission and ecology of the diseases concerned, which will necessitate considerable modifications in future editions. The end of the war will also permit the inclusion of control measures hitherto kept secret.

A most unfortunate misprint occurs in the table giving the characteristics of the rickettsial diseases. scrub typhus is shown as giving a negative reaction with *Proteus OXA* in the Weil Felix test.

Kenneth Mellanby

BABLET J. *La fièvre jaune. Diagnostic différentiel clinique et histopathologique. Hépatite amarille.* [Yellow Fever Differential Clinical and Histopathological Diagnosis. Yellow Fever Hepatitis.] Collection de l'Institut Pasteur. 69 pp. 10 text figs. & 6 figs. (4 coloured) on 3 pls. 1945. Paris. Les Éditions Médicales Flammarion.

The title of this work—Yellow Fever—is somewhat misleading for the greater part and indeed the only section of any value is devoted to a reproduction of the author's observations on the histopathology of the disease [see this *Bulletin* 1936 v 33 333 *et seq.*]

After an introduction stressing the importance of viscerotomy for the examination of the liver in all doubtful cases the author gives a brief summary of the principal endemic centres of the disease at the present time. The view is expressed that yellow fever was introduced from the Antilles and America into South America and West Africa. No evidence is adduced in support of this opinion which is opposed to the generally accepted view that yellow fever was introduced into the Western Hemisphere from West Africa. The account of the symptomatology contains descriptions of a few fatal cases of yellow fever to illustrate what is stated to be a typical form of the disease among Europeans during epidemics also two atypical examples in which the diagnosis was established by histological examination of the liver. There are also brief chapters on clinical differential diagnosis and on the various biological examinations which can be used in establishing the nature of the disease.

The main part of the memoir starts with a historical summary of work on the pathological anatomy of yellow fever. Since 1935 the author has been in charge of the histological examination of the livers of all cases of suspected yellow fever from the French Colonies including the Antilles and Guiana in addition to West and Equatorial Africa. As a result of the study of hundreds of cases he has come to the opinion that the histological changes in the liver furnish the best practical method of diagnosis. Two degenerative processes are constantly in evidence fatty degeneration and necrosis of the hepatic cells. Details are given of the best staining methods and the changes are illustrated by an excellent coloured plate.

The differential diagnosis of the conditions producing liver changes that might be compared with those accompanying yellow fever are then described and illustrated. The most important are the intoxication effects of carbon tetrachloride arsenicals chronic hepatitis spirochaetal jaundice etc. An appendix by Françoise BLOCH and M. R. GODIN contains technical details of the methods used for staining paraffin sections of the liver for the histological diagnosis of yellow fever. The bibliography includes for the most part only publications dealing with the pathology of the disease.

This memoir contributes nothing new to our knowledge of yellow fever and its only value lies in the section on the pathological histology of the liver with its excellent illustrations.

*E. Hinde*

POLAK, Marius Frans. *Vraagstukken der gele koorts. Epidemiologie en vaccinatie* [Problems of Yellow Fever. Epidemiology and Vaccination.] [Thesis for Doctorate of Medicine Univ., Amsterdam, 15 Aug. 1945.] 183 pp. 2 figs. (1 map) & 3 charts. [432 refs.] English summary pp. 160-63. 1944. Amsterdam. NV Noord-Hollandische Uitgevers Maatschappij.

The author of this thesis has made an extended summary of the literature on the subject as his list of 432 references indicates. The book was written in Holland however and few of the papers quoted are dated later than 1940, so that full information was not available to the author on the wartime experience of vaccination in American and British troops and on the epidemic in the Sudan which began late in 1940 and of which only the beginning is here referred to.

The chapters contain information on — Recently acquired knowledge of the epidemiology of yellow fever — an investigation into its spread in Surinam — the modifications in the virus produced by passage in animals — vaccination with attenuated virus — vaccination experiments carried out in Amsterdam with virus 17D — and a comparison between the methods of vaccination with the French neurotropic strain and the American 17D.

Protection tests in Surinam indicate that jungle yellow fever exists there that in the Negroes the men run greater risk of infection than the women, probably because their work takes them more closely into contact with the forest and that in the aboriginal Indians the risks to the sexes are about equal.

*Charles Wilcocks.*

VASSI, Vittorio [Direttore Inc. dell'Istituto di Parasitologie dell'Università di Roma]. *Terapia clinica delle malattie da zoo-parassiti dell'uomo.* [Clinical Therapy in the Parasitic Diseases of Man.] Prefazione del Prof. Vittorio PUGNOLI. 256 pp. 37 figs. 1944. Rome. Editrice Nazionale. [L. 335.]

In the first part of this book the author discusses the general principles of chemotherapy and describes the chemistry and therapeutic action of arsenicals, antimonial, acridine derivatives and other drugs which have a bearing on the treatment of protozoal infections. In a similar section he deals more briefly with anthelmintics, but gives in considerable detail the procedures he advises in the preparation of the patient and the administration of the drugs. In this section male fern, santoun, chenopodium, carbon tetrachloride and other compounds are described.

The second part of the book is devoted to the various diseases in relation to the treatments available and contains some brief notes on diagnosis. The protozoal diseases include those due to intestinal protozoa and to the blood and tissue parasites. American trypanosomiasis is not included. The helminthic diseases include all the common conditions. In a final section are considered myiasis, scabies and pediculosis.

This book was published early in 1944 and was no doubt written before the liberation of Italy. The author was not, therefore, able to consult the most recent work done on some of these subjects by the members of the British and American forces. Nevertheless, one would have expected some reference to the aromatic amine derivatives in leishmaniasis and trypanosomiasis, and a more favourable view of the use of ivermectin in helminth infestation. On the whole

however this is a careful collection of information on most of the known treatments for the conditions with which it deals but it will need considerable modification and amplification in the next edition when the author has had opportunity to assimilate all the work which has recently been done.

Charles Wilcocks

JULIAO Oswaldo Freitas. *Contribuição para o estudo do diagnóstico clínico da lepra nervosa.* [A Study of Nervous Leprosy and its Clinical Diagnosis] [Thesis Fac. of Med. Univ S Paulo 15-1 1945] 203 pp 84 figs. on 28 pls & 12 text figs 1945 São Paulo Industria Grafica José Magalhães Ltda.

A literal translation of the title of this book would fail to convey the extent of the information which it contains. The author has had unique opportunities for observing and studying nervous diseases in general and the nervous lesions of leprosy in particular and he has made the most of these opportunities with the result that he has produced a book which must surely prove to be the last word in nervous leprosy for a long time. It is not a book to be read through or continuously but all practising leprologists should have a copy for ready reference.

The importance the difficulties and the responsibility of making a diagnosis of nervous leprosy are very great. The veriest tyro cannot fail to diagnose leprosy in its developed stages with disfigurements deformities and mutilations or even earlier in the tubercle form. It is in the early stages and above all in the early nerve-stages that difficulties arise and they may be great.

No one could be better qualified than the author to pronounce *ex cathedra* on this question. He possesses for his task the dual qualification of being neurologist to the Department of Leprosy Prophylaxis in São Paulo and at the same time a member of the staff of clinical neurologists of the Faculty of Medicine of the São Paulo University.

The author therefore has abundant material at his disposal and for purposes of description he has divided the work into three sections or chapters but from the nature of the subject these must to some extent overlap. At the same time unless some such subdivision were made it would be difficult to avoid confusion. The first chapter is named the *Nervous Manifestations of Leprosy* and treats in detail with exemplary cases to illustrate them of definite or more or less isolated clinical symptoms such as conditions affecting motility of digits or of larger muscular associations of the limbs affections of the cranial nerves changes in the reflexes superficial and deep of the cutaneous vasomotor system of sweating and of sensory and trophic disturbances—cutaneous atrophy ichthyosis scleroderma 'glossy skin' alopecia onychia perforating ulcer of the sole bone resorption etc.

The second chapter is the shortest of the three occupying 30 pages or one fourth the length of the first. This chapter is concerned with the *Clinical Forms of Nervous Leprosy* and is itself divided to describe three groups of cases: the first according to the localization of lesions neuritis monoplegic paraplegic hemiplegic the second according to the predominance of one or other classes or association of symptoms—sensory motor trophic psychic or mixed thirdly according to the course whether acute subacute or chronic and benign stationary or retrogressing. This chapter ends with an account of diagnosis of nervous leprosy by means of biopsy specimens of the suspected nerve. Examination of these rarely reveals bacteria but the histological changes are fairly distinctive and characteristic—attenuation of the myelin sheaths and Wallerian degeneration. This method is of particular importance

or avoided in any settlement in which the known appropriate preventative measures are applied.

The conclusion to which Swellengrebel's work leads is that if there is any argument valid against the introduction of Jewish refugees as settlers in Surinam it is not the argument of undue danger to their health. The climatic conditions *per se* do not contraindicate white settlement and the incidence of disease for a tropical country is low. The point is made however that small communities lead to inbreeding and that attention should be given to this fact.

Readers of this volume will find in it much that may have a bearing on similar problems elsewhere, though many of the conditions in Surinam are not common elsewhere in the tropics.

Charles Wilcocks.

БОБРИНСКОУ Л. КУЗНЕЦОВ В & КУЗЬКИН А. [Mammals of USSR.] 440 pp 258 figs 32 pls. & 62 maps. 1944 Moscow. Issued by Government Publishing Office Sovetskaya Nauka. [In Russian with an English Preface.]

This is a useful reference book, compiled to aid any person somewhat familiar with the subject to determine the specific name of any of our mammals and to receive a more or less complete information on the geographical distribution of the mammal on the territory of this country though the information concerning the more remote areas is as yet incomplete.

Keys are given, and for each species there are notes on morphology and biology. The geographical distribution is summarized in 62 maps at the end of the volume. There are many line drawings of skull and tooth structure and 32 half-tone plates of most attractive pastel and wash drawings (in monochrome) of the animals in their natural surroundings.

To the epidemiologist the long section on the Rodentia will be of most value.

Charles Wilcocks.

LEAGUE OF NATIONS. Report on the Work of the League during the War submitted to the Assembly by the Acting Secretary-General. Ser L.6 N.P. General 1945 2. 167 pp Geneva. 1945 Oct. [Allen & Unwin Ltd. 40 Museum Street London W C 1.] [2s.] [Review appears also in *Bulletin of Hygiene*.]

The old League of Nations will shortly be replaced by the new United Nations Organisation and the terms of transfer are now under discussion. This report by the Acting Secretary-General, prepared for submission to the League of Nations Assembly which will be convened in 1946 presumably for the last time, describes the work done by the various League Committees and by the Secretariat since 1940 and shows how League organs have adapted themselves to war conditions and how in spite of the breakdown of the political system of the Covenant the non-political technical services have not only survived, but have been performing vital and most valuable duties throughout the war period.

The introductory pages refer to the potential usefulness of the League's activities as a basis for post-war reconstruction and to the problems connected with their transfer to the new United Nations Organisation. An assessment of the value of the League's first "great experiment" in world organization is also attempted.

Chapter 1 of the report deals with the work of the Economic Financial and Transit Department of the League—made easier by the transfer in 1940 of a part of its staff to the United States where a base was set up for observation and intensive research on questions relating to the reconstruction of the world's economic life after the war.

The social and humanitarian activities of the League are then reviewed in Chapter 2 and here an account is given of the work of the Health Organisation which with a staff reduced by 1940 to two doctors—the Officer in charge of the Health Section and the Chief of the Epidemiological Intelligence Service—remained in Geneva to perform the heavy task of preserving what could be preserved of the work of the past and of adapting the efforts of the Health Organisation to the new conditions resulting from the hostilities. In the early years of the war national health services were helped both by direct action and by the supply of documentation and technical advice and reports were prepared for their guidance on such subjects as the medico-social problems arising from the displacement of civil populations. Data were also supplied on a variety of matters including the food ration consumed before and during the war in the occupied countries the foodstuffs most suitable for distribution in concentrated form to the populations of these countries after their liberation and the types of vitamin deficiency disease that were most to be feared.

Later in 1943 the Officer in charge of the Health Service of the League was sent first to London to place at the disposal of the Inter Allied Services the experience acquired by the Health Organisation in connexion with the combating of epidemics the prophylaxis of contagious diseases and assistance for pregnant women and newborn infants and then to Washington to give to the Office of Foreign Relief and Rehabilitation the benefit of the League's nutritional malarial and sanitary engineering experience and to develop collaboration between the League Health Organisation and the Health Division of UNRRA which was in process of organization. Arising from this the League's Health Section established a research unit in Washington in 1944—staffed by its former Chief of the Epidemiological Intelligence Service at Geneva and by the former statistician of the League's Singapore Bureau—which has since become the Epidemiological Intelligence Service of the Health Division of UNRRA.

Meanwhile many of the pre-war long term activities of the League Health Organisation continued including the work on biological standardization on the unification of the national pharmacopoeias and on malaria rabies and nutrition.

After this account of the work of the Health Organisation the remainder of Chapter 2 is devoted to the League's work on the control of the drug traffic international assistance to refugees the settlement of the Assyrians of Iraq and technical collaboration with China.

The remaining chapters deal with Mandates Intellectual Co-operation Questions of a Legal and Administrative Character and the Library at Geneva. The report ends with a list of the League of Nations Publications from January 1st 1940 to October 31st 1945.

This account of the first great experience in international co-operation for peace and human progress goes far to show that the League did not fail it was the nations which failed to use it. If the lesson is learned that however effective the machine may be the outcome will depend on how it is used on the justice wisdom and courage of leaders and above all on the vision and determination of the common people it will have contributed much to the success of the new venture on which the United Nations are now embarking.

R L Sheppard



LEWIS'S MEDICAL, SCIENTIFIC & TECHNICAL LIBRARY Catalogue of Lewis's Medical, Scientific and Technical Lending Library Part I.—Authors and Titles. Part II.—Classified Index of Subjects, with Names of Authors who have written upon them. New Edition. Revised to the end of 1943. pp. 8+928. 1944. London H. K. Lewis & Co. Ltd. 136 Gower Street W.C.1 [To subscribers 12s. 6d. to non-subscribers 25s. (Review appears also in *Bulletin of Hygiene*)]

Lewis's Medical, Scientific and Technical Library is exceptional, if not unique in that it issues regularly in volume form complete and reasonably up-to-date catalogues of the books available in the library. The present edition of Lewis's Library Catalogue has been revised to the end of 1943 and Part I which runs to 714 pages includes some 24,000 titles of books of importance—British, American and English translations of Foreign works—in medicine and science generally arranged alphabetically under Authors names. Part II of the Catalogue provides an alphabetical index of the Subjects covered by the Library with the names of authors who have written upon them. Thus by reference from the authors names given under the subject headings in Part II to the entries under authors names in Part I of the Catalogue readers are enabled to find the full titles dates of publication, numbers of the latest editions, prices and, in the case of foreign books, the places of publication of works on any particular subject of medical or scientific interest. Librarians as well as readers will thus find the Catalogue a most useful source of reference to books published on medical, scientific and technical subjects.

R. L. Sheppard.

TROPICAL DISEASES  
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## SUMMARY OF RECENT ABSTRACTS \*

## III MALARIA

[Continued from p 184]

## Treatment

*General*.—In a comprehensive discussion of the principles governing the curative and suppressive treatments of malaria, especially in relation to military conditions SIMON (p 694) defines subdivisions of the terms prophylaxis suppression and cure and relates the procedures defined under these headings to the state of immunity of the troops (white and non-white) and to the malaria conditions to which they may be exposed. It is not possible further to condense this abstract the author has taken into account all information available on the subject.

FINDLAY *et al* (pp 6 350) in a study of the treatment of malaria in British troops in West Africa, all the infections being due to *P. falciparum* conclude that mepacrine is as satisfactory as quinine or as quinine followed by mepacrine provided that 0.8 gm. is given in the first 24 hours of treatment. No toxic symptoms were seen although some of the patients had been taking suppressive doses of mepacrine for several months beforehand. Quinine however should be used in cerebral malaria, hyperparasitism in the rare cases in which the high temperature fails to react to mepacrine and in the still more rare cases in which mepacrine causes vomiting or psychotic change.

In the *Army Medical Department Bulletin* (p 692) it is stated that a quinine-pamaquin course was more successful than a mepacrine course in the treatment of relapses of *P. vivax* malaria. Subsequent relapses were significantly fewer after the quinine-pamaquin than after the mepacrine course during a follow up period of 5 months. Details are given.

Evidence is brought by CHEN and GEILING (p 348) to show that after intravenous injection quinine and mepacrine are rapidly removed from the circulation by an adsorption process which takes place in the capillaries especially those of the lung. Quinine is rapidly destroyed by enzyme action but the metabolism of mepacrine in the tissues is slow and the process is not yet understood.

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945, v 42. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

In March 1944 TENKIN and RAMSEY (p. 533) issued a monograph on anti-malarial drugs. This is a review of information published in the literature and was compiled as a basis for the revision which the military situation demanded but it does not include the newly-acquired information then restricted to confidential reports, and may therefore be misleading to the student unless this is borne in mind.

**QUININE etc.**—The effect of acid and alkali on the absorption and metabolism of quinine has been studied in animals by ANDREWS and CORWATZER (p. 534) who found that there was no evidence that alkali therapy significantly delayed excretion. The lowered percentage excretion of quinine during alkali administration which has been noted by others was confirmed, but the results are not explained by differences in absorption following administration of acid or alkali. The same authors have studied the rate and degree of absorption from the intestinal tract: the dihydrochloride is more quickly absorbed than the sulphate but differences in the rates decrease with time.

PIRK and ENGELBERG (p. 964) show that administration of quinine has the effect of reducing the prothrombin level of the blood. Soldiers receiving it would therefore be in danger of prolonged bleeding should they be wounded and the authors advocate the concurrent administration of vitamin K in such circumstances.

HEILIG and VESTERGAARD (p. 442) show that quinine when given intravenously on several successive days has a definitely deleterious action on the myocardium, and leads to lowering of the blood pressure probably through an action on the peripheral vessels. They conclude that quinine should not be given intravenously unless there is a specific indication. DREISBACH and HANZLIK (p. 964) agree that quinine given intravenously has a depressant action on the circulation which in cases of severe quinine collapse may be irreversible: they have found that epinephrine, neosynephrine and calcium chloride, when mixed with the quinine, have an action in mitigating this depressant action. Details of dosage are given.

KELLY (p. 861) as a result of a considerable experience in a military hospital, states that a not inconsiderable proportion of blood slides of patients seriously ill from malaria were repeatedly negative for parasites, and that in some fatal cases where this was so sporulating forms were found in the capillaries of the brain post mortem. In the majority of serious cases however the blood was heavily infected. In suspected cases of cerebral malaria, intravenous quinine should be given immediately but for further treatment the author favours intramuscular methyl-sulphonate mepacrine. For cerebral malaria FITZ HUGH *et al.* (p. 340) gave intravenous injections of quinine, well diluted in saline or saline-glucose and administered slowly. As much as 3 or 4 gm. quinine may be given in 24 hours. Intravenous sodium amytal is most useful in convulsions or mania, and spinal drainage in coma. Blood or plasma transfusions are valuable for anaemia or symptoms of shock.

METCALF and UNGAP (p. 341) describe patients with *P. vivax* malaria contracted in the Solomons who had to be repatriated to the United States because of relapses. These men were unable to achieve immunity strong enough to permit them to remain abroad and treatment with mepacrine was not efficacious. The drug of choice was quinine in heavy dosage: there was little advantage in using mepacrine, pamaquin or neocarsphenamine with the quinine. In these men a low degree of parasitaemia was capable of producing a severe rigor.

For the treatment of relapses of *P. vivax* malaria, in men returned to Britain from abroad MANSON BARR (p. 176) advocates the use of Solrochin, a preparation of quinine for intramuscular injection the dose of which contains 0.5 gm. quinine. The injections (two daily for two days) should be followed

by a course of quinine by the mouth and of pamaquin. For *P. falciparum* infections more injections may be needed followed by oral quinine and mepacrine. Solvochin contains antipyrin. HAWKING (p 536) has shown that the lesions it causes in muscle are indistinguishable from those caused by quinine. BROWN (p 779) has found X ray evidence of calcified cysts in the gluteal region of European and Indian soldiers who have received intramuscular injections of quinine. Their appearance is characteristic, but they give no trouble.

RAYMOND (p 250) shows that the totaquina (type I) prepared in Tanganyika Territory contains all the cinchona alkaloids and though in somewhat larger dosage is practically as useful in treatment as quinine. He argues that totaquina of this type is the most economical and effective means of using the anti-malarial action of cinchona bark. A comment in the *East African Medical Journal* strongly supports this view (which indeed is widely held) and urges standardization of totaquina. A controlled experiment carried out by GREEN (p 442) shows that treatment of malaria (chiefly *P. vivax* infections) with totaquina was about as effective as treatment with quinine but that mepacrine was more successful in preventing early relapses than either totaquina or quinine.

RICO (p 177) reports favourably on a gluconate of quinine and calcium in treatment.

The distribution of quinine and other cinchona alkaloids in the fluids and tissues of dogs has been studied by HIATT and QUINN (p 778) for details the original abstract should be consulted. UNTI (pp 90 697) describes a simple method for the estimation of quinine in blood. HIATT (p 178) has determined the plasma concentration of alkaloids of cinchona at various times after a single oral administration.

MERAD and KOPFLI (p 9) discuss the structure of a quinine derivative obtained by allowing rabbit liver to react with quinine *in vitro*.

DAVIDSON (p 964) has found that burasaine (a mixture of alkaloids) has some definite antimalarial properties.

**Mepacrine**—In 1944 the Medical Research Council Committee on Malaria (p 88) issued a statement on mepacrine in which they reproduced a resolution made by the United States Board for the Co-ordination of Malarial Studies. There was very close agreement between the opinions expressed which may be summed up as follows. Under proper administration mepacrine is no more liable than quinine to cause toxic effects. mepacrine is as effective as quinine in the treatment of *vivax* malaria but neither compound will prevent relapses. If properly given mepacrine will practically always suppress and cure *falciparum* malaria, but the action of quinine in this respect is less certain. The Americans point out that mepacrine is effective in suppression [they do not distinguish species in this respect] and that doses of quinine sufficient to produce the same result frequently cause symptoms of cinchonism.

In an important paper on the pharmacological basis of mepacrine therapy in malaria SHANNON *et al.* (p 343) show that the concentration of this drug in leucocytes is more than 200 times as great as the concentration in plasma, and that the ratio between the concentrations in whole blood and plasma varies considerably for a number of reasons. When blood is shed, the mepacrine tends to be released from the leucocytes and it is therefore important that the blood should be centrifuged immediately after withdrawal. If the plasma estimations are not to be vitiated. Most of the mepacrine in plasma is bound to the proteins. In the different organs of the body the concentration of mepacrine varies greatly, being highest in the liver and only relatively small fractions are retained in the plasma. Excretion of mepacrine is slow and accounts for only 1-5 per cent. of the daily dose. degradation is also

slow and mepacrine can therefore accumulate in the body to reach a point of equilibrium which varies in different individuals. Protection against malaria, as noted by HAWKING in comment, is probably achieved at a plasma concentration of about 20 microgm. per litre and this is attained most quickly by high initial dosage. Similarly for treatment a high initial dosage should be used for this mepacrine may be injected intramuscularly but the intravenous route is not advised. Subsequently it should be given by mouth. Details will be found in the original abstract.

MASEN (p. 8) describes a method for the fluorimetric estimation of mepacrine in blood and urine which is sensitive to 0.1 mgm. per litre. Details should be sought in the original. AUERBACH and ECKERT (p. 90) have used a modification of this method which is described.

MARGRAFF *et al.* (p. 251) have shown that the concentration of urinary mepacrine is proportional to that of plasma mepacrine and to that of urinary ammonia so that if any two of these values are known the third can be calculated by means of a simple formula. Plasma concentration, which is a most important factor is difficult to determine but urinary mepacrine and ammonia concentrations can be estimated simply by means of a Lovibond disk. KING and GILCHRIST (p. 781) describe a method for estimating mepacrine in urine for details of which the original abstract should be consulted, and BROWN and BENNIE (p. 780) and MARGRAFF *et al.* (p. 780) have observed that in persons who have been taking suppressive mepacrine for some weeks the plasma mepacrine can be calculated from a formula which takes into account urinary mepacrine, urinary  $\text{NH}_3$ , and a constant. The latter workers (p. 779) show that the error in this procedure is very small, and that the apparatus is simple. The method can be adapted to regimes of mepacrine administration other than suppressive doses but for each regime special measurements are necessary.

YUDKIN (p. 803) describes three simple methods for the estimation of mepacrine in urine for details of which the original abstract should be consulted.

KING and GILCHRIST (p. 782) describe a field method for the estimation of mepacrine in plasma and blood details cannot be given in brief space. The method depends on fluorescence as does that described by HENRY and GRINDLEY (p. 783) for estimation of stilbamidine and mepacrine in urine.

A paper was published in the *Lancet* (p. 342) by the Army Malaria Research Unit, which showed that in estimation of plasma mepacrine the anticoagulant used should not contain ammonia, since ammonia displaces mepacrine from the leucocytes (which have a high concentration of the drug) and therefore leads to grossly exaggerated plasma readings. Potassium oxalate, sodium citrate and heparin are satisfactory anticoagulants.

LEWIS (p. 413) describes a method details of which are given in the original abstract for estimating concentrations of mepacrine in serum. In comment, HAWKING points out that since vastly larger amounts of mepacrine are held in leucocytes than in plasma the separation of serum introduces the probability of error by liberation of mepacrine from the white cells. The ideal is to estimate mepacrine in plasma separated from cells within 15 minutes of withdrawal from the body if this cannot be done mepacrine should be estimated in whole blood, a leucocyte count being made so as to guard against gross abnormalities.

ALLEN (253) points out that patients who have taken large doses of mepacrine may develop a mental condition similar to that of general paralysis, and that a false positive Wassermann reaction may be found, in such cases as a result of malaria. The results that may follow such a mistaken diagnosis are obvious. GASKILL and FRIZ HUTCH (p. 629) report toxic psychosis in 0.4 per cent. of soldiers suffering from malaria and treated with mepacrine most

of these patients recovered. GELLER (p. 9) has not found that relatively large doses of mepacrine produce nervous symptoms. In comment HAWKING states that psychotic symptoms due to mepacrine have occurred but rarely in the wide experience gained in the recent war and that such symptoms usually disappear when the mepacrine is discontinued.

In *Nutrition Reviews* (p. 8) a summary is made of the evidence which shows that mepacrine in high dosage may have a toxic action in animals poorly nourished especially in regard to proteins.

SIEGEL and MUSHETT (p. 178) give an account of the pathological changes induced in animals by administration of large doses of mepacrine. For details the original abstract should be consulted. SIEGEL *et al.* (p. 628) show that very large doses of mepacrine given to rats on a low protein diet caused damage to the liver but in comment HAWKING points out that in man the ordinary suppressive dose does not produce any visceral lesions. In men treated for malaria with courses of mepacrine in fairly high dosage BUTT *et al.* (p. 783) could find no evidence of damage to the liver a conclusion which agrees with that of military investigators in the British Army.

In experiments with young rats HEGSTED *et al.* (p. 784) have found that mepacrine has a thiamin sparing action.

THOMPSON (p. 695) has treated relapses of *P. vivax* malaria with large initial doses of mepacrine with some apparent benefit over courses comprising smaller doses. SMITH and PASSALACQUA (p. 696) also write favourably of the effects of large doses of mepacrine especially in *P. vivax* malaria.

The pharmacological action, especially as regards toxicity of eight salts of mepacrine was studied in animals by BARLOW *et al.* (p. 443). Details should be sought in the original.

BOSE *et al.* (p. 444) show that a butyl acridine derivative (the corresponding amyl acridine compound being mepacrine) has considerable effect in *P. vivax* and *P. falciparum* infections.

*Pamaquin etc.*—WEST and HENDERSON (p. 253) give a list of symptoms which they attribute to the use of pamaquin (plasmoquine) in doses of 0.01 gm daily for 5 days in American troops overseas. These symptoms include jaundice abdominal pain anaemia headache weakness and dizziness. In comment HAWKING observes that it is difficult to exclude other factors as causes of this syndrome and points out that no such complaints were made in a considerable group of British soldiers treated in much the same way.

SHISHLAeva MATOVA (p. 351) produces evidence that the compound Quinolone No. 31 [the chemical name of which is given in the abstract] is about as effective as pamaquin in preventing infection of mosquitoes with both benign and malignant tertian parasites.

*Other Drugs*—COGGESHALL *et al.* (p. 698) have shown that sulphadiazine has no value in preventing relapses in *P. vivax* malaria naturally acquired in the South-West Pacific.

HARNED and ETTELDORF (p. 443) show that sulphathiazole can be administered concurrently with quinine or mepacrine. In malarious districts such a combination is necessary when bacterial diseases and malaria co-exist.

KAY (p. 696) found no advantage from giving three injections of Mapharsen in conjunction with mepacrine in the treatment of relapsing *P. vivax* infections. On the other hand DAO (p. 697) reports good results from the use of this drug alone in *P. vivax* infections infections being given at intervals of 4 to 7 days for courses of eight injections.

HINDLE *et al.* (p. 446) have found that penicillin is without effect in malaria.

### Suppression.

FINDLAY and STEVENSON (p. 349) recount the history of drug suppression of malaria in West Africa during the war. Quinine in 5-10 grain doses was not satisfactory; mepacrine (0.4 gm. each week) was better but the best results were obtained with mepacrine 0.1 gm. daily except on Sundays. Figures are given which demonstrate these facts beyond doubt. The only cases of cerebral malaria were in men who either had not taken mepacrine or had taken it irregularly. The use of mepacrine appeared to reduce the number of cases of blackwater fever. [The findings in West Africa are therefore in line with those of workers in New Guinea.]

FAIRLEY (p. 656) comments on the high rate of malaria experienced by the troops in New Guinea before the use of suppressive mepacrine became universal. To test the suppressive and therapeutic effectiveness of mepacrine, quinine and certain sulphonamides FAIRLEY (p. 630) and his associates made very careful investigations on healthy volunteers in Australia. These men were infected with Papuan strains of *P. falciparum* or *P. vivax* and were subjected to most rigorous conditions. The author makes the point that no instance was seen of failure to infect the normal white man unless he was protected by a drug. The sulphonamides suppress *P. falciparum* but not *P. vivax*; mepacrine in a daily dose of 0.1 gm. suppresses and will cure *P. falciparum* infection if continued for some weeks after exposure but though it suppresses it it will not usually cure *P. vivax* infection. Quinine is not nearly so effective. Institution of suppressive mepacrine as a routine and made a disciplinary measure in the troops in New Guinea brought about a most dramatic reduction in the incidence of malaria but the problem of relapses of *P. vivax* after cessation of mepacrine administration remains. In this work it is shown that though blood is infective for a few minutes after infection by bite it becomes uninfected until the 7th (*P. falciparum*) or 9th (*P. vivax*) day; sporozoites are apparently rapidly removed by macrophages and fixed tissue cells.

In the *Royal Naval Medical Bulletin* (p. 179) recommendations made in the United States Navy for the use of mepacrine as a suppressive are reproduced. These follow the accepted dosage of 0.1 gm. daily and the point is made that the treatment should be commenced a month or more before arrival in the malarious area or that if time is short 0.2 gm. daily for a week should be taken to build up the necessary blood concentration.

McCoy (p. 785) sums up the use of mepacrine for suppression of malaria, in doses of 0.1 gm. daily. Symptoms of intolerance usually pass off quickly. They very rarely persist. It is necessary to attain the required plasma concentration by administration for some time before exposure to malaria, and it may be necessary in military operations to continue administration for some time after cessation of exposure. There is no evidence of the production of mepacrine-resistant strains of parasites as a result of long-continued administration.

From investigations in Lebanon MEASHAM *et al.* (p. 695) conclude that mepacrine though not a true prophylactic is a useful suppressant, and that if continued long enough it cures infections at a subclinical level.

Suppressive treatment with mepacrine and pamaquin given on two successive days every 5 days was found by LEITMAN (p. 254) to be useful in the prevention of malaria in Tashkent. In a comparison of the effects of mepacrine alone and of mepacrine together with pamaquin in adult doses of 0.3 gm. and 0.03 gm. of the two substances weekly scaled down for younger persons PARROT *et al.* (p. 445) found that neither was effective in preventing malaria in the inhabitants of a hyperendemic area of Algeria.

MACGRAITH and HAYARD (p. 863) made long and detailed studies on some 500 volunteers in relation to the effects of mepacrine taken in suppressive doses. They concluded that the drug is both safe and effective. As a result of careful examination of 102 soldiers DREW and REID (p. 862) think that prolonged administration of mepacrine in suppressive doses does not lead to any cumulative toxic action and that there is good reason to believe that its protective action is very great. McCORKLE (p. 536) concludes from an investigation that prolonged administration of mepacrine in suppressive doses has no deleterious action on the liver and in comment HAWKING states that elaborate investigations in Britain have led to the same opinion.

RUSSELL (p. 630) produces evidence which suggests that mepacrine in suppressive doses tends to produce some degree of eosinophilia.

ROMERO MOLINER (p. 180) shows that in Fernando Po a daily dose of 0.4 gm. quinine was not an effective suppressive. Atepe (containing mepacrine and pamaquin) was much more successful.

### Control.

In an address on the need for a malaria control policy for rural Africa MACDONALD (p. 965) claims that in spite of the relative immunity attained by Africans after the age of childhood malaria still continues to be a cause of ill health in adult life and he is not content with the view that it is unwise to attempt malaria control because anything less than complete control would interfere with immunity. He advocates experiments on a large scale in which all the methods now available should be used together with improvement of the whole circumstances of African life. ANNICKS *et al.* (p. 966) on the other hand restate the argument that incomplete control would make matters worse in the hyperendemic areas. They see more hope from improvement of environmental conditions and nutrition so that the Africans may be more able to resist malaria than from control by methods now used. They too advocate continued research and experiment on a large scale but think that the means of control now available are not likely to give satisfactory results in the areas concerned and under existing conditions. A single and cheap form of attack is required.

SYMES and HADAWAY (p. 785) have made a detailed investigation of the effect of DDT in solution or as an emulsion in killing adult mosquitoes in dwellings in British Guiana. The results were very good and the residual action most notable—in one area the reduction of anophelines (compared with control houses) was 89.9 per cent. 7 weeks after application. *Anopheles darlingi* is more susceptible than *Culex fatigans* to DDT. Discharge into the open air is also effective but needs investigation. The authors note that in the daytime *A. darlingi* frequents ground shaded by vegetation and that ground-spraying is therefore essential.

RICE *et al.* (p. 632) show that Thianite, a terpene thiocyanate ester incorporated in DDT sprays greatly increases the immediate knock-down effect—the residual lethal action however is due to DDT.

EDDEY (p. 255) describes the programme of spray-killing of adult mosquitoes (chiefly *A. gambiae*) which was undertaken in Takoradi during the war. The best results were obtained with pyrethrum aerosol and pyrethrum in kerosene (DDT evidently not being available). The procedure was popular and malaria rates are quoted which suggest that there was a substantial reduction of incidence as a result of this measure.

Dusting of African huts with pyrethrum powder at the rate of 2 ounces per 1 000 cubic feet twice each week was found by GARNHAM and HARPER (p. 447) to reduce by about 50 per cent. the amount of malaria in a village in Kenya at an altitude of 5 000 ft., in which transmission was largely seasonal.



Senior WHITE and VENKAT RAO (p. 180) have made an extensive study of the daily movements of *Anopheles* of the *flavirostris* group (*flavirostris minimus* and *parvus*) in relation to houses baited with man or animals, and of the effects of spraying (at various intervals) on the older (and potentially infective) mosquitoes. The rationale of spraying is to destroy the mosquito before it becomes infective, i.e. before the 9th-14th day according to the time of the year. The authors therefore suggest that spraying should be spaced so that any mosquito will twice run the risk of being hit before its glands become infected. By daily spraying the density of mosquitoes was (in one experiment) reduced 24 fold by intermittent spraying, with intervals of not more than 2 days 6-fold. The oocyst and sporozoite rates of the mosquitoes caught did not vary much but it is by the reduction of density that malaria control is achieved. *A. culicifacies* however can be controlled by weekly or at most twice weekly spraying. For details the original abstract should be consulted.

GILROY and CRAWFORD (p. 789) describe their method of draining that part of the foreshore near Lagos, which is covered by the sea only by high tides, and in which there are many crab holes and shallow pools. This zone is the chief breeding place of *A. melas*. By constructing an embankment on the seaward side of this zone and draining the zone by one-way gates through the embankment the authors effected a marked fall in anophelines over a large area; the malaria rate also fell, but there may have been additional reasons for this notably the removal of the local population of gametocyte carriers.

COLLIGNON (p. 686) reports on anti-malarial measures taken in the Department of Algiers during 1943.

Emulsions of mineral oils have successfully been used in larval control by KANCHAVELI (p. 632).

WASICKY and UYTI (p. 182) have tested DDT in a colloidal preparation, as a larvicide. A dilution of 1 in 50 million kills mosquito larvae in 24-36 hours and there is a residual action in gradually diminishing potency for several weeks.

ROZENOOM and HESS (p. 182) show that there is a close positive correlation between the production of *A. quadrimaculatus* and the extent of intersection line between plants, water and air. High intersection line values conduce to increased oviposition and decreased larval mortality. HESS and HIXEN (p. 183) describe the means by which the breeding of *A. quadrimaculatus* is controlled on the great reservoirs of the Tennessee Valley Authority. By bringing the water level to full during winter or spring, and then reducing to summer level, much of the floatage is stranded and rendered harmless. Later a constant level reduces the amount of subsequent marginal vegetation but from the beginning of moderate *quadrimaculatus* production weekly fluctuation of level eliminates the intersection line and produces a clean shoreline. The permanent works undertaken for the control of *Anopheles* breeding on the Kentucky reservoir of the Tennessee Valley scheme are described by BISHOP and GARTRELL (p. 184) who show that in projects of this kind such works are more economical than the larvicidal and shore line maintenance programmes which would have been necessary had they not been done. Details must be sought in the original.

A description of technical methods in the use of aeroplanes for dusting with Paris green is given by KRUSE *et al.* (p. 184). This method of mosquito control is largely used in the Tennessee valley. METCALF and HESS (p. 357) note that when Paris green is used from aircraft, only about 25 per cent. reaches the treatment area, the rest being dispersed by wind and propeller action. They found that if particles of larger size (20-50 microns) than usual are employed there is a 60 per cent. increase in the amount which reaches the treatment area, and that particles of these sizes are, in fact ingested by larvae of *A. quadrimaculatus*. They therefore recommend the use of larger particles.

SCHOOF (p. 537) shows that non-baited anopheline houses—rough wooden structures easily made and transported—afford the most useful means of observing adult *A. quadrimaculatus* in relation to control measures.

MULRENNAN *et al* (p. 633) quote instances of potential malaria vectors from foreign countries being found in the United States and comment on the need for strict supervision of aircraft which may bring such dangerous species.

### *Malaria of Birds and Monkeys*

BROOKE (p. 864) gave to canaries diets in which there were certain deficiencies comparable with deficiencies in human diets in parts of the United States and elsewhere. He observed the effect of these diets on the course of infection with certain bird malaria parasites in general this was to cause the birds to suffer from more severe primary attacks and to reveal a greater tendency to relapse and a reduced resistance to superinfection. Biotin deficiency increases the severity of certain avian malarial infections but SEELER and OTT (p. 540) produce evidence that riboflavin deficiency has rather the opposite effect.

SEELER (p. 699) has found that administration of pyridoxime definitely inhibits the action of quinine and mepacrine in certain malaria infections of ducklings but does not influence their toxicity. It is not known how pyridoxime acts in this respect.

WRIGHT and SABINE (p. 252) discuss the effect of mepacrine on the oxygen consumption of tissues and HAAS (p. 252) has investigated the effect of mepacrine and quinine on isolated respiratory enzymes. Readers are referred to the original abstracts for the results of these highly technical studies.

SPECK and EVANS (p. 967) have shown that *P. gallinaceum* like *P. knowlesi* forms lactic acid from glucose. They discuss the action of quinine and mepacrine on the metabolic activities of *P. gallinaceum* in relation to therapeutic activity. SILVERMAN *et al.* (p. 448) have studied the metabolism of *P. gallinaceum* *in vitro* but for details of this intricate work the reader should consult the original abstract.

A comprehensive description is given by HUFF and COULSTON (p. 538) of the development in chickens of *P. gallinaceum* from sporozoite to erythrocytic trophozoite. The sporozoite whether injected by syringe or mosquito bite develops in macrophages divides into cryptozoic merozoites which in turn give rise to metacryptozoic merozoites which enter either other macrophages or erythrocytes. A later stage of development consists of the formation of larger numbers of small (micro-) merozoites and at this stage there is a sudden flooding of the blood with erythrocytic forms. The only species of malaria parasites in which cryptozoites have been found are those in which abundant exo-erythrocytic stages occur. It should not be assumed that all species of *Plasmodium* must develop in the same way. This description of the development of *P. gallinaceum* is the first complete account which has been given.

CANTRELL and JORDAN (p. 633) have found all species of *Aedes* tested to be susceptible to *P. gallinaceum* infection. *Culex pipiens* is resistant.

HAAS and EIVING (p. 539) have succeeded in infecting chick embryos with *P. gallinaceum* by inducing infected mosquitoes to feed through the shell membrane. HAAS *et al.* (p. 865) have devised a technique for making serial passages of *P. gallinaceum* in chick embryos. They note that a green discoloration of the membranes amniotic fluid yolk liver and spleen is diagnostic of malarial infection.

COATNEY *et al.* (p. 865) discuss the results of experiments on infection of chicks with *P. gallinaceum* either by the bite of a single infected *Aedes aegypti* or by injections of sporozoites or of comminuted whole mosquitoes. The last is the method of choice for inducing infection for studies in chemotherapy.

non-malarious areas 10.8 for larger spleens the rates were 11.1 and 3.2, a significant difference. It would seem that PDI spleens [palpable on deep inspiration only] should be disregarded in surveys of places of low malaria endemicity. Palpable spleens were slightly more frequent in children with a history of recent illness, measles, chickenpox, etc., than in other children.

It is interesting to note that, ignoring spleens palpable only on deep inspiration, enlarged spleens were more frequent in New York children 3.7 per cent. than in Massachusetts children, 1.0 per cent. Both localities are free from endemic malaria.

Nearly all the children examined were between 5 and 12 years of age.

Norman White

SPICER S. S. The Spleen Survey as applied to the Measure of Malaria in the United States—a Review of the Literature. *J. National Malaria Soc.* Tallahassee, Fla. 1945 Sept., v. 4, No. 3 165-82. [Numerous refs.]

During the war a thick blood film survey was carried out throughout the endemic malaria areas of the United States. 100 000 thick films were examined. Less than 0.2 per cent. of these were positive, and nowhere was the rate high enough for checking the results of malaria control measures. At the same time in Florida 20 to 25 per cent. of school children were found to have palpable spleens though less than 1 per cent. had positive blood smears. Partly to explain this situation, the author has made a study of the literature to determine the value of splenometry in the conditions of low endemicity prevailing in the United States. Among the results of the inquiry are the following conclusions—

A recent epidemic of one of the childhood diseases, and possibly a high rate of infections of the upper respiratory tract, may increase the spleen index. A proportion of apparently healthy children have spleens that are palpable on deep inspiration. Spleen rates as high as 15 per cent. may occur in the absence of malaria—these will be almost all PDI spleens [palpable on deep inspiration only]. Spleen rates above 15 per cent. are probably significant of malaria. A fall in the malaria rates over several years causes a quicker decline in parasite rates than in spleen rates. The spleen index in a community may remain high for several years after a malaria epidemic, partly as a result of relapses, and thus reflects the rate of transmission during the preceding several years. Quinine medication causes a reduction in spleen mass. Spleen rates are influenced by race, age and parasite species. Greater enlargement occurs in the white than in the coloured race, and in children than in adults.

Norman White

SAUTETAS L. Paludisme autochtone. L'épidémie de Camargue. [Indigenous Malaria—the Camargue Epidemic.] *Rev. Paludisme et Méd. Trop.* 1945 Apr. 15-May 15 v. 3 No. 15-16, 81-3

This is a brief account of an epidemic of malaria in Camargue in 1943 and is based on a report published by J. SAUTET in the journal *Marseille Médical*. Camargue is the region enclosed by the two main branches of the river at the mouth of the Rhône—the only French delta. The inhabitants have always led a somewhat precarious existence in this low-lying tract, with its numerous marshes of varying degrees of salinity. Mosquitoes are abundant and malaria was endemic, but the disease had been very little in evidence during the previous decade—local inhabitants said that it had almost disappeared. The outbreak reported occurred in September 1943. There were 177 cases recorded among the inhabitants of les Saintes-Maries-de-la-Mer and adjacent farms, hospital patients at Arles. Annuité labourers employed in the recently created

rice-fields Russo-Polish workers and young workers who had come to help gather the grape harvest Sautet considered that this number represented not more than half the real incidence. All were *P. vivax* infections of an extremely mild type which showed no tendency to relapse Blood examination showed gametocyte carriers to be exceedingly rare this, according to Sautet is characteristic of places in which malaria is in process of disappearing The vector was *A. maculipennis* var. *cambojensis* it was abundant but not noticeably more so than in previous years The local population blamed the ricefields but the vector species was not found breeding there The indigenous population of Camargue has evidently a high degree of resistance to the local strain of *P. vivax* The author suggests that susceptible arrivals should take prophylactic quinine during the transmission season.

Norman White

GUHL R. Zwei Falle von autochthoner Malariainfektion in der Schweiz [Two Cases of Autochthonous Malaria in Switzerland.] *Schweiz. med. Woch.* 1946 Jan 26 \ 76 No 4 67-9 1 fig. [14 refs]

POLUNORDVINOV A D [Highland Malaria in Southern Tadzhikistan.] *Med. Parasit. & Parasitic Dis.* Moscow 1945 \ 14 No 2 18-20 [In Russian]

The author reports the occurrence of endemic malaria due to *Plasmodium vivax* *P. falciparum* and *P. malariae* at altitudes up to 2750 and 2850 metres (= ca. 8,920-9,248 feet) above sea level in the mountains of Southern Tadzhikistan (Middle Asia) These altitudes represent practically the limit of human settlement in the region in question.

C A Hoars

GARCIA SASTRE L. Notas sobre el paludismo en la isla de Gran Canaria. [Notes on Malaria in the Island of Gran Canaria.] *Rev. Sanidad e Hig. Publica* 1945 Apr \ 19 No 4 257-71 7 figs. (2 on 1 pl.)

It is almost certain that malaria has existed in the Island of Gran Canaria since very ancient times Recorded information as to its extent and distribution is scanty Climatic conditions are eminently favourable for anophelines and travellers records of 1775 and 1803 refer to the great prevalence of tertian fevers in the island. Parts of it however remain free from malaria. In the capital Las Palmas no anophelines were found among 18,826 mosquitoes examined the few cases of malaria that occurred there in 1944 were all due to infections contracted elsewhere. In the south and centre of the island malaria has long been endemic Medical reports refer to the large spleens and earthy complexion of some of the inhabitants notably the children, but without other noteworthy clinical manifestations of malaria.

During the last three months of 1941 an outbreak of malaria occurred in a labour force engaged on construction work between Fataga and Maspalomas There were 77 cases The source of infection may have been a man who contracted malaria in the neighbourhood of Seville. No further cases were reported during the first eight-months of 1942, but the closing four months of that year witnessed a second outbreak of 113 cases in localities adjacent to the infected area of the previous year In June 1943 malaria reappeared in the north-east and south west of the island and the ensuing epidemic involved 8 of the 21 administrative divisions. In all 2164 cases were recorded in 1943 the highest incidence being in the middle of the southern half of the island. During 1944 cases were reported in every month of the year in fact there was only one week in February in which no new case was notified. The total cases for the year numbered 3,978 and 13 of the 21 *municipios* were involved. Once again the *municipios* of San Bartolomé and Santa Lucia, in the south and centre suffered

most here the incidence was equivalent to 190 and 180 per 1,000 of the population. The north-east of the island escaped. The maximum incidence in 1944 was in September 971 cases, and the lowest in February and March, 28 cases each. Some of the greatly increased incidence in 1944 as compared with the previous year may have been due to the fact that the local medical profession had become more malaria-minded as the result of circulars, propaganda and the like. Of 3,406 cases in 1944 *P. vivax* was responsible for 1,722, *P. falciparum* for 1,680 and mixed infections for 24. *P. malariae* was not observed.

Work with regard to the malaria vectors has not been completed. It would seem that the vectors belong to the *Anopheles* group probably *A. hispaniola* and *A. sergenti*. Although no anopheline breeding could be found in the urban area of Las Palmas, important breeding places were found in four localities at distances of no more than from 6 to 12 kilometres away.

In view of the rapid spread of infection to places that have been hitherto immune it is not unlikely that the whole island will soon be involved.

NORMAN WHITE

NÁJERA, L. La fauna anofelica de las islas Canarias. [The Anopheline Fauna of the Canary Islands.] Reprinted from *Boletín de la Real Soc. Española Hist. Nat. Madrid*, 1944, v. 42, 325-6.

The author notes that no anophelines were mentioned by BECKER (*Dipteren der Kanarischen Inseln und der Insel Madeira*, Berlin, 1908) and that the only species found later have been *A. hispaniola* (by Graham) and *A. sergenti* (by Christophers). He writes of a collection of mosquitoes recently acquired from a collector in the islands and now deposited in Madrid. CHARLES FITCHES.

LE GALL, R. Le paludisme en Afrique Occidentale Française au Togo et à Madagascar en 1941. [Malaria in French West Africa, Togo and Madagascar in 1941.] *Bull. Office Internat. d'Hyg. Publique*, 1944, Mar.-June, v. 36, Nos. 5-6, 203-24.

This report brings together information concerning the prevalence of malaria during 1941 in each of the Colonies of French West Africa, the mandated territory of Togo and in Madagascar. As elsewhere in the world, complete statistical information regarding mortality caused by malaria is non-existent. The ratio of malaria cases treated to the total number of sick persons seen in hospitals, dispensaries, infant welfare centres, travelling dispensaries, etc., varies somewhat from year to year and provides some indication of the fluctuations in malaria incidence. Such information suggests that malaria was somewhat more prevalent in 1941 than in either of the two previous years, but the differences were not great. In Madagascar exceptional rainfall was responsible for very severe malaria—one third of all sick persons treated were suffering from that disease.

Of special interest in the report is the reference to an inquiry that was carried out in the Comores archipelago, which lies to the west of the northern tip of Madagascar. Malaria was found to be endemic in all the islands, but in varying degrees of severity. Mayotte and Mohéli are the islands most severely affected. In Mayotte spleen rates varied between 40 and 80, and parasite rates from 10 to 18. In Mohéli, there were spleen rates of 50 to 80 and parasite rates of 20 to 35. *P. falciparum* infections were predominant. Anjouan is the island least affected—spleen rates varied from 20 to 35. *P. vivax* infections were found in the elevated parts of the island. Great variations of endemicity were found in the island Grande Comore—variations determined in part by the nature of anopheline breeding places, the most important of which are the tanks providing

the water supplies of villages. The three species of *Anopheles* found were *A. gambiae*, *A. funestus* and *A. mauritanus*, the first two being vectors of malaria. These three species are also found on the adjacent north west coast of Madagascar.

Norman White

VISWANATHAN D. K. Studies on Malaria in Infants in North Kanara District, Bombay Presidency. *J. Malaria Inst. of India* 1945 June v 6 No 1 1-38 4 charts

The observations recorded were made in Haliyal population 6 448 and Yellapur population 1 926 in the North Kanara District where *A. fluviatilis* is the malaria vector. During the space of one year the blood of 432 infants was examined 1 628 examinations in all. On the average 45 per cent. of the total infant population were examined each month. The results indicate that the transmission season in Haliyal is confined to the four months September to December. In Yellapur transmission occurs throughout the year except during the monsoon months July to October. *P. vivax* and *P. falciparum* infections were equally prevalent. *P. malariae* was much less in evidence than it had been in the previous year when malaria was less severe than in the year of investigation. The parasite density in infants was lower than in children of the 2 to 10 age groups but gametocyte prevalence indicates that infants play an important part in transmission.

Malaria in these two places appears to be responsible for an increase in the number of stillbirths and premature births and for increased neonatal mortality resulting from maternal malaria. It is also an important direct cause of infant mortality. The infant mortality rate of Haliyal was 192 per 1 000 live births.

The author sets out the results of his inquiry in very great detail and discusses at length the value and limitations of such data as he collected in assessing malarial endemicity.

Norman White

YACOB M. & SWAROOP S. Investigation of Long-Term Periodicity in the Incidence of Epidemic Malaria in the Punjab. *J. Malaria Inst. of India* 1945 June v 6 No 1 39-51 5 charts

In the absence of reliable data as to the causes of death in the Punjab the authors make use of the deaths ascribed to fevers in their elaborate study of malaria periodicity in that Province. Malaria epidemics in the Punjab occur soon after the rainy season and any inordinate increase in deaths ascribed to fevers during the last three months of the year affords in the absence of other unusual epidemics presumptive evidence of excessive malaria mortality. In studying the fluctuations of malaria mortality from year to year use is made of an epidemic figure which is the ratio of the average monthly number of deaths from fevers during October, November and December to the monthly average of fever deaths of April, May, June and July of the same year. In years of low malaria incidence the epidemic figure should approximate unity.

Epidemic figures for 77 years (1867 to 1943) have been studied. A statistically significant decrease of malaria mortality over this period has been demonstrated and there is a strong indication that epidemics of malaria tend to occur after a period of about eight years.

Norman White

FARINAUD E. & PROST P. Impaludation et prémunition dans les régions de paludisme endémique de l'Indochine méridionale. [Malarial Infection and Premunition in Endemic Regions of Indo-China.] *Bull. Soc. Path. Exot.* 1944 v 37 Nos 3/4 93-7

KAN HUI-CHIEH. Malaria Incidence in Two Districts in Western Chekiang, China.  
*Chinese Med J* Washington. 1944 Oct.-Dec. v 62, No 4 311-13

Kwon C. S. A Preliminary Report of Malaria Survey in Kweichow China  
*Med J* Washington. 1944 Oct.-Dec. v 62, No. 4 314-19

FAUST E. C. Clinical and Public Health Aspects of Malaria in the United States from an Historical Perspective. *Amer J Trop Med* 1945 May v 25  
No. 3, 185-201 5 figs. (3 maps & 2 graphs) [41 refs.]

This is an informative and interesting account of the introduction, spread and decline of malaria infection in the United States since infection was introduced with the advent of European explorers and settlers and the importation of slaves from Africa two hundred years ago. There is no indication that malaria existed anywhere in North America before then. In the middle of last century most of the settled part of the United States was highly malarious but even then the hyperendemic centres of infection were in the South. Thereafter with increasing prosperity more intensive cultivation, and greatly reduced cost of quinine the heavily endemic territory began to shrink into the south-east corner of the States. Between 1915 and 1933 there was but little change in the malaria incidence except for the five-to-seven years cycle of revived intensity. The severe economic depression commencing in 1931 was responsible for a great increase in the intensity and distribution of malaria. This stimulated co-ordinated control measures which appear to have been responsible for the remarkable decline in malarial mortality which has been continuous and almost uninterrupted since 1933. This decline has been described by the author in annual reports which have been summarized in this Bulletin.

The malaria situation in the United States of military forces, merchant seamen and civilians from highly malarious regions is discussed. Both *A. quadrimaculatus* and *A. freeborni* have been shown to be capable of transmitting Pacific and Mediterranean strains of *P. vivax*.

An interesting graph shows how completely malaria was controlled among troops in the United States during the recent world war and the remarkable decline in malaria mortality in the army overseas in 1944 as compared with 1943.

BRITISH GUIANA. Report of the Malaria Investigations Service of the Medical Department, British Guiana, for the Half Year July-December 1944  
[GIGLIOLI G. Government Malariaologist 48 cyclostyled pp. [14 refs.]

This progress report contains a vast amount of tabulated information concerning spleen and parasite rates in many parts of British Guiana, and the distribution of *Anopheles*. The special report on the incidence and distribution of malaria throughout the colony which is in course of preparation, will be of great interest. [The Report for 1943 was summarized in this Bulletin 1945 v 42, 614]

A survey of the Corentyne Coast was carried out in September and October 1944. Malaria endemicity here is low of 1163 children examined only 1.3 per cent. had enlarged spleens. Parasites were found in 10.7 per cent of 200 children. In the positive blood preparations parasites were few in the majority. Prolonged examination of thick films revealed only one or two ring forms. *A. aquasalis* (*luridus*) is very prevalent in this area, and *A. albipennis* also occurs. Neither of these species appears to be of any importance in the spread

of malaria in British Guiana. Wherever human settlements exist livestock is abundant, and both of these species show a marked preference for the blood of livestock. No *A. darlingi* were found on the Corentyne Coast.

An appendix to the report by M. KENNY deals with inadequate screening as an important factor in spreading malaria. At a mining centre on the Berbice River the population lived in screened wooden houses and in temporary open camps. In the screened houses were numerous cracks and other openings in the floors walls and roofs and the doors were often left open after sunset. Hundreds of mosquitoes were captured in the screened houses 83 per cent being anophelines nearly all *A. darlingi*. Blood examination of the occupants showed a parasite rate of 36 per cent and very numerous gametocyte carriers. Oöcytes were found in 88.8 per cent. of the *A. darlingi* examined. After the institution of daily mosquito catches and the treatment of human carriers the percentage of infected mosquitoes quickly dropped to less than one per cent. The imperfectly screened houses had been mosquito traps. Norman White

HENDERSON J. M. A Discussion on Caribbean Malaria Control. *J. National Malaria Soc.* Tallahassee Fla. 1945 Sept. v 4 No 3 189-200 5 figs

This is a short general survey of malaria conditions prevailing in the islands of the Greater and Lesser Antilles and in the Guianas. The author directs attention to the large amount of research work that remains to be done the multiplicity of problems awaiting solution and the opportunities the Caribbean offers to the enthusiastic malarialogist. Norman White

CAUSEY O. R. & MELLO G. B. Malaria in the Amazon Valley of Brazil during 1942 and 1943. *Amer. J. Trop. Med.* 1945 July v 25 No 4 323-7 1 map & 1 graph

Hitherto but little information has been published regarding malaria in the Amazon Valley a fact which enhances the interest of this contribution. The Brazilian portion of the Amazon valley elliptical in shape covers 3,800,000 square kilometres. The country is remarkably flat. Belem near the coast is 14 metres above sea level. The elevation of Iquitos Peru 3,200 kilometres up the valley is only 100 metres. Much of the land is flooded. The population of about 1,500,000 live mostly near the navigable rivers in huts built in piles above the mud and water in small villages on knolls surrounded by water or in towns on upland plateaux. Rarely do the people attempt to grow their own food there is usually a food shortage with consequent malnutrition made worse by widespread intestinal parasite infestation. There are wet and dry seasons but rain falls in every month. The average annual rainfall in Manaus is 1,995 mm. and in Belem 2,805 mm.

A malaria parasite survey was made in December 1942 a season when malaria rates are expected to be at their lowest. Thick blood films were taken from about 6 per cent. of the population of Belem, from about 20 per cent. of the population of small towns with more than 1,000 inhabitants and from 30 per cent. of the population of smaller towns. The survey was restricted to towns accessible by air boat or train. In all, 19,629 blood smears were examined. malana parasites were found in 979 a parasite rate of 5 per cent. For children of the 1 to 9 age group it was 7.1. *P. falciparum* infections numbered 407 and *P. vivax* 573.

The second survey was carried out at the end of the wet season in June 1943 when 27,103 persons from 37 towns were examined. Instead of the expected rise in incidence the survey showed a parasite rate of only 3.3 per cent. This



may be due to the fact that after the first survey large quantities of atabrin were distributed throughout the valley and anti-mosquito work had been started in several localities.

*Anopheles darlingi* is the chief vector of malaria throughout the valley. *A. aquasalis* another vector is found near the coast. *A. darlingi* is dependent on lakes or ponds for its survival during the dry season. In an exceptionally dry season these may dry up and *A. darlingi* may disappear altogether. There are some malaria free areas which may be so explained. When reintroduced, *A. darlingi* may cause severe epidemic malaria in such places. Norman H. kite

BRUG S. L. Exo-Erythrocytaire malariparasieten. [Exoerythrocytic Malaria Parasites.] Reprinted from *Nederl Tijdschr v Geneesk* 1941 June 14 v. 85 No. 24 2745-52 2 pls. (1 coloured) & 1 chart. [Numerous refs.] English summary (8 lines)

The paper describes certain intracellular bodies which were found in smears of the lung of a case of general paratyph which was treated by infection with *Plasmodium inaa*. Death occurred ten days after the intravenous inoculation of the parasites and six days after the first appearance of these in the patient's blood. They were also present in the blood at the time of death. A post mortem examination was made two days after death the body having been kept meanwhile in the cold chamber. Smears were made from a number of organs but it was only in a smear of the lung that anything resembling exoerythrocytic developmental forms of the malarial parasites was found. Three such forms illustrated in a coloured plate and in microphotographs were found, all within cells of the endothelial type. The smallest form was a darkish blue body 3-4 $\mu$  in diameter containing four large and three small red-staining masses. It lies in the cytoplasm of a cell about 20 $\mu$  in longest diameter. The other two forms which are in somewhat larger cells are of a different nature. They were both found in the same microscopic field. The cytoplasm of each cell is dotted, over the greater part of its extent by red-staining masses some of which are the size of those in the small structure first described others are larger and some are smaller. The cytoplasm of the cell is not uniform, areas of dark blue being interspersed with less deeply staining areas. In some cases a darkish blue ring is associated with one of the red masses giving a resemblance to a malarial ring. The number of red masses in each cell: 40 to 50.

The question asked by the author is: are these appearances due to the presence in endothelial cells of malarial parasites or are they the result of cell metabolism? It is remarkable that the three forms described are the only ones seen in all the films examined after many hours of search, and that the two large ones were in the same field. In the larger forms there is no clear demarcation between parasite and cell but this might be due to the fact that segmentation into separate merozoites had already occurred and that their outlines are somewhat obscured—a not unusual appearance in the case of the multiple infection of the cytoplasm of large cells by small parasites. It is perhaps a coincidence if the red bodies are nuclei of merozoites that both the larger cells contain parasites in the same stage of development.

However this may be it is clear that the illustrations bear a striking resemblance to appearances which may be seen in smears of organs containing the exoerythrocytic forms of hard malarial parasites. [The reviewer has re-examined certain of his own films which show these developmental forms and he has to admit that had the forms depicted by the author occurred in these films he would not have hesitated to call them exoerythrocytic forms but this is in films in which many of the parasites show a clear demarcation between

the cell cytoplasm and that of the parasite so that the occurrence of others in which this demarcation is less clear would not be remarkable. A point worthy of note is that in the cytoplasm of the cell containing the small parasite there are two or three red bodies which cannot be of a parasitic nature though they bear a resemblance to the red bodies in the other two cells. A resemblance of certain blue areas to malarial rings has been mentioned but malarial merozoites in endothelial cells are not of the ring form which is the stage adopted only after invasion of the red blood corpuscle. On the whole therefore the reviewer agrees with the author that the structures which are the subject of his paper bear a resemblance to exoerythrocytic forms of bird malaria but that it is impossible to assert dogmatically that they are the corresponding stages of development of *Plasmodium vivax*. The author is to be congratulated on his exhaustive search and on the coloured drawings which illustrate his paper and which are undoubtedly faithful representations of the cells they depict.]

BOYD M F On Difficulties arising in the Experimental Propagation of *Falciparum Malaria*. Amer J Trop Med 1945 July, 25 No 4 293-306

*Plasmodium falciparum* has been used at the Florida State Hospital since June 1932 largely for the inoculation of coloured patients. The continued propagation of this species by natural passage has proved much more difficult than that of *P. vivax*. Breaks from inoculation failures have occurred in all strains used. In a closely reasoned paper the author analyses the conditions in which these difficulties have arisen.

Failures to infect have occurred though the mosquitoes used were subsequently shown by dissection to have been infected. The presence of sporozoites in mosquitoes that fail to infect indicates that the gametocyte level in the patient from whom the mosquitoes were infected is not a factor. Resistance of the patient has not often been responsible for failure as was shown by the results of subsequent reinoculations. Increasing age of sporozoites (the period elapsed since the completion of the extrinsic incubation period) has been associated with an increasing proportion of failures but failures have occurred with quite young sporozoites. It would appear that the recent ingestion of quinine by the patient on whom the mosquitoes are infected may impair the vitality of the resulting sporozoites.

When some of the strains used were propagated by intravenous inoculation of infected blood their capacity for producing gametocytes deteriorated, sometimes suddenly sometimes gradually. The phenomenon is not attributable to the resistance of the patient or to the administration of quinine. The deterioration persisted through subsequent passages.

A summary does small justice to this paper

WATSON R B Observations on the Transmissibility of Strains of *Plasmodium vivax* from Pacific War Areas by *Anopheles quadrimaculatus*. Amer J Trop Med 1945 July, 25 No 4 315-21

Norrian White

Six strains of *P. vivax* were obtained from soldiers who had presumably acquired their infections in Pacific war areas by injecting their blood into patients requiring malaria therapy. Morphologically five of these strains differed in no way from the indigenous McCoy strain in general use for treatment but the ring forms of one strain resembled *P. falciparum* trophozoites. The subsequent development of amoeboid forms revealed their identity. Some of the patients with histories of previous *P. vivax* infections offered considerable resistance to the Pacific strains four patients being refractory

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*A. quadrimaculatus* were fed on these patients with Pacific infections. Sporozoites were found in mosquitoes fed on patients infected with three of the six strains. The failure of three strains to infect mosquitoes may have been due to the climatic conditions prevailing at the time of experiment. It was excessively hot and dry, temperature 84°F and relative humidity 53 to 56. Sporozoite transmission of three strains was successful. In some cases mosquitoes were infected, though microscopic examination revealed no gametocytes at the time of the infective feed.

It is concluded that some at least of the Pacific strains of *P. vivax* can be transmitted by *A. quadrimaculatus* which seems to be, however, a somewhat less efficient vector of these strains than it is of the McCoy strain.

Norman White

Watson R. B. On the Probability of Soldiers with Pacific *Plasmodium vivax* Malaria Infecting *Anopheles quadrimaculatus*. J. National Malaria Soc. Tallahassee, Fla. 1945 Sept. v. 4 No. 3 183-8.

Batches of 25 newly emerged *A. quadrimaculatus* were applied to patients with *P. vivax* infections, acquired in the Pacific war area, without regard to gametocyte levels. After incubation for 15 days in an air-conditioned room these mosquitoes were examined for salivary gland infection. For 1428 mosquitoes fed on 117 cases (87 patients) the infection rate was 11.8 per cent. The highest infection rate was obtained in mosquitoes which had been fed on patients with parasite relapses without fever. Individuals experiencing their 6th to 15th relapses were twice as likely to infect mosquitoes as were individuals with earlier or later relapses.

Norman White.

ROUSSEAU E. Influence du développement plasmodien sur la fécondité des moustiques hôtes. [The Influence of Plasmodial Development on the Fecundity of Mosquitoes.] Bull. Soc. Path. Exot. 1945 v. 38, Nos. 9/10 300-304

CRUCA, M. BĂLĂȘ L. CHELĂRESCU M. & CRISTESCU A. Capacité d'infection du sang des porteurs de gamétocytes de *Plasmodium falciparum* pour *Anopheles maculipennis* (1 atroparvus) [Infective Capacity of *Plasmodium falciparum* Gametocyte Carriers for *Anopheles maculipennis atroparvus*.] Reprinted from Bull. Sect. Sci. Acad. Roumaine. Bucharest. 1942, v. 25 No. 2, 98-102.

Thirty-six *P. falciparum* gametocyte carriers were used for the infection of laboratory bred *A. maculipennis atroparvus*. Twenty-three of these patients had been infected with virulent blood, 9 had been infected with sporozoites and 4 were cases of natural infection. The strain used for the infection of 32 patients had been kept going for 14 years in the malaria-therapy station.

The researches show that 50 per cent. of these gametocyte carriers were capable of infecting a lot of mosquitoes in the conditions of the experiment (one infecting feed only). Two cases on which mosquitoes were fed 10 times show the importance of the number of infecting feeds in producing infection.

The infective power of the blood is independent of the manner in which infection was contracted (virulent blood or sporozoites). Three of the four gametocyte carriers who had naturally acquired infections successfully infected mosquitoes, a very much higher rate of infectivity than that shown by patients infected with the laboratory strain. The vitality of the gametocytes of these naturally acquired strains appeared to be much higher than of those of the therapy strain.

Norman White.

GARNHAM P C C The Role of *Anopheles pharoensis* Theobald in the Transmission of Malaria in Kenya Colony Ann Trop Med & Parasit 1945 Oct. 10 v 39 No 2, 63-5

*Anopheles pharoensis* is a carrier of malaria in Egypt the Sudan Uganda the Belgian Congo and Southern Nigeria in Egypt it is an important carrier in Northern Nigeria and Kenya no infections have been found  
*A. pharoensis* has a patchy distribution in Kenya at altitudes between 2 000 and 3 000 feet It breeds in large numbers in swamps around lakes and also in overgrown drains and streams. Adults are rarely found in large numbers in human dwellings At Kisumu where the observations recorded were carried out, they formed from 0.7 to 4 per cent. of the total anopheline day catches in huts for night catches the percentage was 10 They mostly enter huts between midnight and dawn. The salivary glands of 1,334 female *A. pharoensis* and 33 midguts were examined. Neither sporozoites nor oöcysts were found. The species feeds on man the stomach contents of 10 engorged females all gave positive precipitin reactions with anti human serum The maxillary index of local specimens was 14.6 which suggests zoophilism. The length of life of the species is sufficient to develop infection. The author suggests that where *A. pharoensis* is an important vector of malaria, a variety of the species and not the type-form is concerned.  
 Norman White

VINCKE I PARENT M BERTEAUX M & DE MEULENAERE J Note sur la biologie de *Anopheles duren* Edw [A Note on the Biology of *Anopheles duren* Edw] Bull Ass Congolaise des Anciens Etudiants de l'Université de Liège 1945 Oct No 5 30-39 1 chart.

*Anopheles duren* is a common day biting mosquito near Elizabethville in the Belgian Congo It is not found at all in human habitations but is commonly captured among trees near water Biting takes place throughout the hours of daylight but ceases completely at nightfall other species for instance *A. funestus* were observed during the same investigation to bite almost entirely by night.

Dissections were made of 736 adult *A. duren* some on the day of capture some after five days captivity Approximately 9 per cent were infected with malaria parasites most of them having salivary gland infections

Larval breeding places are described. Shaded sections of rapidly running streams are the most important. Both larvae and adults are commonest in January and February and scarcest from March to September

Kenneth Mellanby

WEATHERSBEE A A. & BOHART G E. Observations on the Nocturnal Activity of *Anopheles* and certain other Mosquitoes in Eastern Puerto Rico. Puerto Rico J Pub Health & Trop Med 1944 June v 19 No 4 626-34 1 chart.  
 [Spanish version 635-42.]

Three experiments were conducted in an attempt to determine the time of greatest activity of mosquitoes in an area of Eastern Porto Rico  
 Horse baited traps were established in three localities and hourly collections were made from them from 5 p.m. until morning The first experiment ran from October 30th to November 10th 1942 the second from November 18th to 29th 1942 and the last from January 19th to 30th, 1943

Three species of *Anopheles* were taken *A. albimanus* (1,330) *A. grabhami* (347) and *A. vestitus* (32) There were also five species of *Culex* three *Aedes* two *Psorophora* and one *Democrilus*

The hourly figures are tabulated and show that *Anopheles albimanus* was more active between 8 p.m. and 3 a.m. than during either the earlier or later hours and that the peak time of entry lay between 10 p.m. and 1 a.m. The numbers of the other anophelines do not indicate any pronounced peak of activity.

The common mosquitoes *Culex bahamensis*, *nigripalpus*, *quinquefasciatus* [sic], *Aedes taeniorhynchus* and *Psorophora ferox* readily entered the traps at all hours of the night. H. S. Lesson.

RUBENSTEIN, A. D., SHULMAN, M. H. & MERRILL, D. The Hazard of Transfusion Malaria after the War. *New England J. of Med.* 1945 Aug. 23 v. 233 No. 8, 234-7.

Since 1929 twelve cases of post transfusion malaria have been reported in Massachusetts. On the assumption that the chance of such happenings may be increased in the future owing to the greater number of potential donors who have served in malarious regions the authors give details of the twelve cases that have occurred to emphasize the risk of post transfusion malaria. Of the 12 infections 9 were due to *P. malariae*, 2 to *P. vivax* and one to an undetermined species. The interval between the transfusion and the onset of symptoms varied between 10 days (*P. vivax*) and 111 days (*P. malariae*). The time elapsed since the donor was last in an endemic malaria region was determined in 5 cases: the longest period was 27 years, the shortest 12 years. Attempts to demonstrate malarial parasites in blood smears of the donors were made in 7 cases but were successful in only two. Norman White

TALICE, R. V. & MACKINNON, J. E. Paludismo accidental por transfusión [Transfusion Malaria. Arch. Uruguayos de Med. Ciruj. y Especialidades 1945 Nov. v. 27 No. 5 473-81. 29 refs. English summary.]

"Two accidental cases of transmission of malaria by transfusion of whole blood are recorded.

Both cases were produced by *Plasmodium malariae*.

One of the donors acquired malaria in Africa 9 years before and the other in Italy 7 years before.

"The infective area of malaria endemicity does not reach the Republic of Uruguay. Consequently in order to avoid accidental transmission of malaria the authors emphasize the advice and conclusions given by Hutton and Shute which may be easily accomplished in Uruguay: that only donors who have never left the country should be used.

CIUCA, M., BALIU, L. & CHELARENCO, M. Contribution a l'etude de l'immunité dans l'infection paludéenne expérimentale. Observations recueillies sur 41 sujets immunisés. Contribution to the Study of Immunity in Experimental Malaria Infection. Observations on 41 Immunized Individuals. Reprinted from Arch. Roumaines Path. Exper. et Microbiol. Bucharest, 1943 Jan. Dec. v. 13 No. 1/2, 45-122, 41 figs. [111 refs.]

The receipt of this interesting study, admirably produced, affords welcome evidence that the scientific work of CIUCA and his colleagues triumphantly surmounted difficulties imposed by war conditions and has been most profitably carried on.

The paper opens with a useful summary of contributions to the literature of acquired immunity against human, bird and monkey malaria. The 111 references in the bibliography are an indication of the comprehensiveness of

this summary [Some recent work was evidently inaccessible to the authors for example BOYD & KITCHEN (1943) this *Bulletin* 1943 v 40 818 is not quoted]

The observations recorded relate to 41 patients who after having been submitted to malaria therapy were kept under control for from 4 to 14 years. They were immunized by repeated inoculations of virulent blood or more rarely of sporozoites. After the period of immunization inoculations were suspended for some years during which time monthly examinations of blood were made. The duration of immunity was gauged either by determining the persistence in the body of parasites by transfusion of blood into a susceptible individual, or by a direct test of the immunity by a fresh injection of virulent blood.

*P. malariae* confers a more lasting immunity than the other two species of human plasmodia. The persistence of an immunity against *P. malariae* in the absence of parasites from the body detectable by transfusion certainly does not rule out the possibility of a humoral or cellular immunization. In the immunity conferred by *P. vivax* the rôle of preimmunization is more in evidence but in 3 of 14 of the cases recorded immunity persisted though no latent infection could be demonstrated. When the higher frequency of positive transfusions in *P. vivax* infections is considered it must be remembered that the patients were not protected from possible fresh natural infections.

From the point of view of efficacy and duration of immunity conferred by repeated inoculations *P. falciparum* comes last. The severity of this infection necessitates earlier antimalarial treatment after the first inoculations. The infection is of shorter duration than the other two and there is therefore a shorter antigenic saturation of the organism. All the same a certain resistance persists in patients immunized with *P. falciparum* inoculations as evidenced by the fact that spontaneous recovery may take place from infection given several years later.

HUNTER T A A Fever in a Hyper-Endemic Malarial Area. A Critical Analysis of 2,913 Cases. *Indian Med Gaz* 1945 May v 80 No 5 247-55 Norman White

A forward Treatment Unit in one of the most malarious areas of the Assam Burma border in the height of the transmission season received up to capacity all cases of fever British and Indian in which no definite diagnosis had been made. Diagnosed cases of malaria were also received but these were few in number. There were in all —

Proved malaria Clinical malaria Not malaria	British	Indian	Total
	643 41 177	1 563 45 444	2,206 (76%) 86 (3%) 621 (21%)

The author protests against the diagnosis of clinical malaria and the commencement of antimalarial treatment before diagnosis has been confirmed. Of the cases of clinical malaria admitted as such not more than a sixth eventually justified that diagnosis. The facile diagnosis may be dangerous in this series five cases of pneumonia were overlooked by a too easy resort to it. Severe types of malaria are relatively uncommon 2.4 per cent. in this series and fulminant types are rare. In all severe cases parasites were plentiful in the peripheral blood. No evidence was forthcoming of the existence of that

"bogey man of the medical officer" the cerebral case of malaria with persistently negative blood slides. The thick drop method of blood examination is very sensitive. In the series of cases reported, parasites were found on the first examination in 81 per cent. of British cases and in 90 per cent. of Indian cases on second examination, 12 hours later parasites were found in a further 8 and 6 per cent. respectively. There is moreover in military practice an important practical objection to the diagnosis of malaria on insufficient grounds. A patient suffering from malaria is absent from duty for 15 days the average non-malaria patient in this series was fit for duty again within the week.

The percentage incidence of species of plasmodia in this series were —

	<i>P. falciparum</i>	<i>P. vivax</i>	<i>P. malariae</i>	Mixed
British troops	30	64	1	6
Indian troops	43	47	1	9

Most British troops had been taking mepacrine as a suppressive most Indian troops had not. This may have been a factor in determining the greater relative prevalence of *P. falciparum* among Indian troops.

In nearly two-thirds of the malaria cases the spleen was not palpable. The spleen rate was higher among Indians.

In 70 cases in which a suspicion of malaria persisted after three negative blood examinations, adrenaline injections were used as a result parasites were found in seven patients. Adrenaline is a useful diagnostic aid. Sternal puncture, a simple procedure was used 20 times. It was not useful as an aid to diagnosis. Spleen puncture was performed three times. It revealed one *Leishmania donovani* infection and one mixed *P. falciparum* and *P. vivax* infection. The procedure is, of course, not suitable as a routine diagnostic measure.

Only eight British and four Indian patients developed cerebral symptoms. There were no algid cases and there were no deaths. A dose of quinine was given intravenously without delay to all patients with *P. falciparum* infections who had symptoms of any degree of severity or in whose blood there was high parasite density.

Norman White

BYSTROV P. V. [Malignant Fulminating Tertian Malaria, according to Observations of Tambov Pathological Department.] *Vest. Parazit. & Parazit. Dis. Moscow* 1945 v. 14 No. 2, 21-5. [In Russian.]

The author in 1927 was the first to draw attention to the occurrence in the Soviet Union of a fulminating deadly type of benign tertian malaria, affecting chiefly children. Since then outbreaks of this form of malaria have been regularly recorded. This *Bulletin* 1943 v. 40 436-688. 1944 v. 41 257-823. In the present paper the author records post mortem observations on 100 fatal cases of *P. vivax* malaria, carried out by him in the course of the last 20 years, at the prosectorium of the Tambov hospital. Outbreaks of this form of malaria occur regularly every year in the spring (March, April, May) the majority of cases being in children between the ages of 4 and 16 though in seven cases the victims were adults.

The clinical picture was similar in all known cases. The majority had previously suffered from malaria, and usually the attack which culminated in death was the second one. This attack—which was accompanied by repeated vomiting followed by loss of consciousness, convulsions and death—usually started suddenly and lasted only several hours. In all cases the diagnosis was confirmed

by the finding of typical *P vivax* in the blood and organ smears the predominant stages being schizonts. The histopathological picture revealed no special features. In distinction to the comatose form of malignant tertian malaria, the brain never showed any macroscopic evidence of pigmentation. Among the characteristic changes the author notes (1) enlargement of the spleen (2) cerebral oedema, and (3) increased intracranial pressure. Microscopical examination reveals a moderate number of parasites and slight pigmentation chiefly in the spleen and liver. The enormous accumulations of these elements, characteristic of malignant tertian malaria, are never observed.

The author attributes the grave symptoms and fatal termination in this form of malaria to an acute cerebral oedema accompanied by increased intracranial pressure which leads first to irritation and finally to paralysis of the nerve centres. This effect may be due both to mechanical and chemical causes, while the oedema itself is visualized as a local allergic reaction on the part of the nervous tissue as the result of sensitization by the products of decomposition of foreign proteins provided by the parasites

C A Hoare

COGGESHALL, L. T. *Malaria and Filariasis in the Returning Serviceman. The Ninth Charles Franklin Craig Lecture. Amer J Trop Med* 1945 May v 25 No 3 177-84

The information in this lecture is based on observations of more than 3 000 service men returned from overseas in the Marine Barracks Klamath Falls Oregon. Most had acquired malaria in the Pacific war area. The records show that initial infections had frequently been with *P falciparum*, but only *P vivax* infections were found at this station. Three men, who had been admitted for filariasis experienced their first malarial attack on the station where there is no possibility of local infection. In one of these cases eight months had elapsed since the man had been in an endemic area and had discontinued suppressive mepracrine. Infections with Pacific strains of *P vivax* are very prone to relapse. Fifty-seven per cent of the men under observation had had more than 14 acute attacks—some had had as many as 40. The recrudescences have a certain rhythm—many men could predict within a week when the next attack would occur. There was a remarkable absence of malarial cachexia. Splenomegaly was noted in less than 5 per cent. of the men even after 20 to 30 recrudescences. Immediately after the acute attack spleens were palpable in about 8 per cent. Anaemia was conspicuous by its absence—after six weeks at the station (the altitude of Klamath Falls is 5 000 feet) the average red blood count was 5,300 000. Except for persistent headache in some cases there was no disability between acute attacks of fever. Finally Negroes who are very refractory to U.S. strains of *P vivax* are very susceptible to Pacific strains.

The men were put on full duty, military training, recreational, educational and vocational activities. This was regarded as important. Physical fitness was quickly regained and the development of hospitalitis avoided. Even South Pacific malaria is a self limited disease. The rate of recrudescence had a downward trend in the malaria that was still active after three years from inception.

There was a large group of men with *Wuchereria bancrofti* infection which in 96 per cent. of cases had been contracted in the Samoan group of islands. The incubation period from the first possible exposure to infection to the appearance of initial symptoms averaged nine months. The clinical signs were lymphoedema, lymphadenopathy and lymphangitis—in the neck (2 per cent.) upper extremities (30) lower extremities (9) scrotum (1) spermatic cords (15) and testes (18 per cent.) The manifestations were very mild. Microfilariae were not found in any man in the station—occasional eosinophilia was the only abnormal



finding on blood examination. Temperatures were normal, and a chronic cough was the only symptom. Occasionally the oedema, lymphangitis and muscular soreness flare up but for a few days only and attacks become less and less frequent. It has been necessary to admit to hospital only one man in 800 for filariasis. The psychic element in these cases is prominent and patients need reassuring—all accumulated evidence shows that filariasis will not result in permanent disability in such cases. Mental and physical rehabilitation of these cases is most important to avoid unnecessary invalidism.

There is no likelihood that filariasis will gain a foothold in the United States. [See also ZELIGS, this *Bulletin* 18:6 v. 43 53] Norman White

KAPLAN A. Recurrent Headache resultant from Malaria. *J Amer Med Ass* 1945 Oct 27 v. 129 No. 9 612 13

An American Marine who had apparently been exposed to malarial infection in the Pacific area between April 1942 and the time of his admission to the ship's sick bay in December 1943 complained of severe occipital headaches of three weeks' duration which prevented sleep and had led him to drink alcohol to excess in the hope of getting some relief.

Very thorough physical and psychiatric examinations, radiography of the skull, Kahn tests of the blood and cerebrospinal fluid, chemical examination of the blood and cerebrospinal fluid, the extraction of two lower molar teeth, all led to no diagnosis during two months of hospital study; he was discharged unimproved and at his own request returned to duty. No examination of blood films for malaria parasites was made.

His headaches continued and prevented sleep and after trying to carry out his duties for five days he was again admitted for further study. This produced no diagnosis except one of psychoneurosis by the psychiatrist who reported fully on his mental state. Again no blood films were examined. After two months he was admitted to a hospital on the mainland and was again submitted to exhaustive physical and psychiatric examination together with laboratory studies, but still no examination of blood films was made. The psychiatrist reported that the patient had a desire to do his duty but showed lack of energy and determination—he appeared to be unhappy.

After a month's leave he was allowed to return to duty and managed to carry on for nine months in spite of recurrent headaches. He was then returned to the Pacific area where his headaches continued for eight months and he steadily lost weight for six months. He was admitted to the hospital complaining that his headaches had been very severe for the last month and that he had had chills and fever for 10 days. A blood film showed *Plasmodium vivax*. Treatment with quinine and atabrine cured the chills and fever and his headaches completely disappeared—for the first time during some years.

The author comments that the experience he describes is not altogether unusual and that malaria in the Pacific area is a common disease.

J. F. Corson

NAGLEY L. Probable Relapse of Malignant Tertian Malaria after Thirteen Years. *Lancet* 1945 Dec. 15 773-4

This is a report of a most unusual case. The patient had been a soldier in India from 1919 to 1928 when he returned to England and since then he has not been out of the British Isles. He had malaria in India in 1928 and a possible relapse in 1932 which was "cured" with one dose of quinine. Thereafter he remained in good health till April 1935 when he fell ill with jaundice, vomiting, bloody diarrhoea and daily shivering attacks. Blood examination

revealed very numerous ring forms of *P. falciparum* and crescents. He recovered. It is incredible that he should have been infected with *P. falciparum* in England thus early in the year. He had never been treated with malaria therapy nor had he ever had a blood transfusion. It is difficult to escape the conclusion that the attack was a relapse 17 years after infection.

Norman White

Bissow H. Über Psychosen nach Malaria. [Malarial Psychoses.] *Allgemeine Zeitschr. f. Psychiatrie u. ihre Grenzgebiete* 1944 Sept. 25 v. 123 Nos. 3/4 235-77 [18 refs]

More than half of this long article consists of a detailed description of the symptomatology of 14 cases of malarial psychoses of which 10 were associated with benign tertian infection three with malignant tertian and one with a mixed benign tertian and malignant tertian.

All the patients were being treated or had been treated with the standard course of atehrin and plasmoquine but the author does not consider that the treatment was responsible for the illness.

No indication is given of the total number of cases of malaria among which the psychoses occurred except that the author refers to an extensive experience of great epidemics during the war and mentions that the condition is relatively uncommon.

In five cases the onset was during a febrile paroxysm in eight it occurred one to nine days after defervescence and in one it was 20 days later. The manifestations were very varied including mania anxiety depression hallucinations delusions and in three cases suicidal tendencies.

The duration was very variable but even in prolonged attacks the prospect of complete recovery is considered to be good.

John W D Megaw

Menon T B. & Vellath G D. Acute Polyarteritis Nodosa in a Case of Malaria. *Indian Med Gaz* 1945 Sept. v. 80 No 9 452-4 7 figs on 1 pl. [12 refs.]

Babin Frances & Dulaney Anna D. Complement Fixation in Malaria and Syphilis. *Amer J Hyg* 1945 Sept. v. 42 No 2 167-73 3 figs

The authors have found that not only may malaria be a cause of false positive complement fixation reactions for syphilis but that syphilis may be a cause of false complement fixation reactions for malaria when a phosphate buffer extract of *P. knowlesi* is used as antigen. The human material available for study consisted of 200 patients with relapsing *P. vivax* infections who were clinically and serologically negative for syphilis. 408 sera giving positive Kahn reactions obtained from the laboratory of a State Health Department and 22 syphilitic patients with induced malaria. Sera were collected at intervals of 3 to 5 days from the malaria patients. 1851 samples were thus collected and on each sample complement fixation tests for both malaria and syphilis were performed simultaneously. Of these 129 gave positive Wassermann reactions (7 per cent) and 112 of these 129 sera also gave positive results with the *knowlesi* antigen (87 per cent). Of the 1722 sera that gave negative Wassermann reactions 1105 (64 per cent) gave positive malaria reactions. Most of the positive Wassermann reactions in malaria patients occur from 6 to 10 days after a malaria attack.

Of the 408 syphilitic sera taken at all stages of syphilis infection 14.5 per cent. gave strongly positive reactions and 6.8 doubtful reactions with the *knowlesi* antigen. High titred syphilitic sera give a larger number of these false reactions than do low titred sera.

In the 22 syphilitic patients with induced malaria the malaria complement fixation test became positive at the time the first positive blood film was observed, or shortly after and the titres followed the rise and fall of the parasitaemia. Eighteen of these 22 patients showed a rise in Wassermann titre coincident with the rise of the malaria complement fixation titre. The relation between fluctuations in the malaria and syphilis complement-fixation titres was striking.

Norman White.

ROBINSON H. M. Jr & MCKINNEY W. W. The Effect of Vivax Malaria on Spinal Fluid and Blood Serologic Test for Syphilis. *J Amer Med. Ass.* 1945 Nov 3 v 129 No. 10 667-8 1 chart.

One hundred soldiers who were suffering from *P. vivax* malaria, with parasites in the peripheral blood, and who were non-syphilitic, were arbitrarily selected for these studies. They had all been in a malarious region for several months and had been transferred to a malaria free district three months before the investigation began. Nine were experiencing their first attack of malaria the others had had from one to sixteen previous attacks. Lumbar puncture was performed and blood taken for serological tests within 5 days after the diagnosis of malaria was made. If the blood test was positive or doubtful the test was repeated at weekly intervals till a negative reaction was obtained. The standard three-tube Kahn flocculation test was performed on all blood specimens and the spinal fluid was examined with the standard Kahn test Pandy and cell count. The spinal fluid Kahn reaction was negative in all cases. In two cases the Pandy was reported as "a trace". The cell count was within normal limits in all. The blood serological test for syphilis was positive in 33 patients doubtful in 11 and negative in 56. Two of the patients with positive reactions were lost from observation. Of the remainder 28 gave negative reactions after four weeks and all had become negative after 10 weeks. All patients had been put on mepacrine therapy as soon as the diagnosis of malaria was made. There was no apparent correlation between the number of attacks of *P. vivax* malaria suffered and the development of positive serological reactions for syphilis.

Norman White.

BRUNETON, W. L. Malaria Therapy in Syphilitic Primary Optic Atrophy. *J Amer Med. Ass.* 1946, Jan. 5 v 130 No. 1 14-16 3 figs. [Refs. in foot notes]

FENTON J. C. B. & IKKES J. A Staining Method for Malaria Parasites in Thick Blood-Films. *Trans. Roy Soc Trop Med & Hyg.* 1945 Sept., v 39 No. 1 87-90

The staining method described is a modification of the now well-known Field procedure whereby a thick film is dehaemoglobinized during the staining process which is completed by immersion for 10 to 15 minutes in a corrective Leishman solution. It is claimed that the method ensures optimal staining results for the demonstration of malarial parasites. Those who wish to try the new method must consult the original article for details of the technique and method of preparation of the three staining solutions used.

C. M. Wexson

DAS GUPTA, B. M. LOWE, J. & CHAKRAVARTY H. M3349 (Paludrine) in the Treatment of Human Malaria. *Indian Med Gaz.* 1945 May v 80 No. 5 241-5.

This study of the value of paludrine an antimalarial compound prepared by Imperial Chemical Industries in the treatment of malaria, was designed to

determine the toxicity of the drug and the relapse rate after treatment. The difficulty of keeping general hospital patients under observation sufficiently long to determine the relapse rate prompted the selection of malaria patients in the Narkeldanga Relief Camp for Sick Destitutes for the trial. Thirty-one such patients were admitted into the Tropical Diseases Hospital and 75 were treated in the Camp. It is rather unfortunate that patients in such bad physical condition should have been selected.

The drug was put up in tablets each containing 0.2 gm. The dose recommended in the control of attacks of malaria was three tablets a day for seven days. The occurrence of two deaths of patients under treatment in hospital early in the trial caused the subsequent dosage to be reduced to two tablets a day. The two patients who died were both infirm men of 60 and 65 years of age, their weights were 88 and 85 pounds respectively. Whether the toxicity of the drug contributed to death seems to be doubtful.

The authors conclude that paludrine has an action comparable to that of quinine and mepacrine in both *P. falciparum* and *P. vivax* infections, fever being promptly controlled and parasites disappearing from the peripheral blood. In four cases of *P. malariae* infection the action was less marked.

Of 60 patients treated and kept under observation for several weeks, 18 had a clinical relapse from 19 to 58 days after treatment, and seven had a parasitic relapse without fever. The early relapse rate was thus 30 per cent. Some of these relapses may well have been fresh infections for most of the work was done in a camp in a highly malarious area in the middle of a malaria epidemic!

Of 51 patients with *falciparum* infections and observed for several weeks there was no *falciparum* relapse, but 8 had a return of fever with *P. vivax* in the blood.

In persons in reasonable physical condition symptoms of intolerance to the drug (such as nausea and vomiting) are slight and present no great difficulty. In persons with complicating diseases, particularly respiratory diseases, the danger of toxic effects is much greater. Three deaths occurred among patients being treated with two tablets a day. Thus there were five deaths in all, but in only one of these was there no serious complicating disease.

Norman White

STOKES J. F. The Treatment of Relapsing Malaria. *J. Roy. Army Med. Corps* 1945 Aug. v. 85 No. 2 75-80 1 fig. [13 refs.]

The drain on man-power of continually relapsing malaria is more serious than the occasional death from cerebral malaria. The relapse rate in a series of British patients of the 14th Army known to be relapsing was 64.7 per cent. over a period of 11 weeks. The author discusses various views that have been put forward regarding the pathogenesis of relapse. In a search for a method of reducing the relapse rate a trial was made of urea stibamine. This was prompted by certain analogies between kala-azar and malaria, but more by two cases that had come under observation. These were two Indians who were suffering from both kala-azar and relapsing malaria, neither had a malaria relapse while undergoing prolonged treatment with urea stibamine.

Two series of observations were carried out: the first on Indian soldiers, 48 experimental and 50 controls, and the second on British troops, 52 experimental and 52 controls. The observations were made in malaria-free localities.

Every patient received the standard malaria treatment: quinine 10 grains thrice daily for 2 days; mepacrine 0.1 gm. thrice daily on days 3 to 7; pamaquin 0.01 gm. thrice daily for British troops and twice daily for Indian troops on days 10 to 14. The experimental patients received doses of urea stibamine

on the 15th, 17th, 19th and 21st days of 0.05, 0.10, 0.15 and 0.20 gm. respectively. The corresponding doses for Indian troops were 0.025, 0.05, 0.10 and 0.15 gm.

The relapse rates for the control and experimental groups of British troops were almost identical over a period of 91 days: 70.6 and 70.2 per cent. On the other hand urea stibamine appeared to reduce the relapse rate of the Indians who were however observed only for 5 weeks. During this time the relapse rate of the control group was 34 per cent. and of the experimental group 6.25 per cent. But in the experiment with British troops 46 per cent. of the relapses occurred after the fifth week and the author believes that had the Indians been kept longer under observation the relapse rates of the two groups would have more nearly approximated.

The author concludes that urea stibamine is unable to influence the course of relapsing malaria.

Norman White

PROKOPEAKO L. L. Parasite-carriage of *Pl. vivax* in a New Focus of Malaria subjected to Control Measures. *Ud. Parazit. & Parazit. Dis.* Moscow 1945 v. 14 No. 2, 3-13, 4 figs. [In Russian.]

This paper deals with the effect of systematic drug treatment upon the incidence of carriers among patients suffering from benign tertian malaria in a new focus of the disease. The observations were made in three villages of the Moscow province during 1940 and 1941. Both clinical cases and carriers were treated with acrinone mepracrine, the course consisting of three cycles of seven, two and three days respectively, separated from each other by free intervals of ten days each, the daily dose for adults being 0.3 gm. During the entire period of observation the number of cases of malaria with febrile symptoms exceeded that of asymptomatic carriers (249 or 79.6 per cent. and 64 or 20.4 per cent. respectively, out of a total of 313 cases). The effectiveness of the treatment was assessed by comparison of 141 patients who had undergone a regular course of treatment on the one hand and a group of 46 treated irregularly on the other hand. In the former group relapses occurred only in 19.8 per cent. while in the latter 26 (i.e. more than 50 per cent.) relapsed. Furthermore in the first group repeated relapses were more frequent: thus 28 patients had 37 relapses comprising 23 acute and 14 asymptomatic cases (carriers). In the second group 28 patients had 48 relapses (27 acute and 21 asymptomatic). It is concluded that properly conducted regular treatment of malaria leads to a marked reduction in the total number of relapse cases, both acute and asymptomatic.

C. M. Hoare

GALESHKINA O. V. Malaria Treatment by Irradiated Quinine. *Ud. Parazit. & Parazit. Dis.* Moscow 1945 v. 14 No. 2, 26-7. [In Russian.]

It has been shown by R. SKIN that quinine irradiated by ultraviolet rays has a more powerful effect upon cultures *in vitro* and a more lasting therapeutic action in bird malaria, than ordinary quinine. In the present paper the author records the results of treatment of human malaria with irradiated quinine. The method of preparation is as follows: 10 per cent. solution of quinine hydrochloride is poured out into Petri dishes and irradiated with a quartz lamp at a distance of 30 cm. for five minutes. The solution is then evaporated in a water bath, and the dry powder is administered in daily doses of 0.3 gm. for four days in succession (five days in the case of malignant tertian malaria) followed by three cycles of three days each with intervals of four days between the cycles.

Of the 30 patients under this treatment 20 were in the acute stage of the disease with parasites in their blood (17 benign and 3 malignant tertian cases) while 10 had subfebrile temperatures attributed to chronic malaria though no parasites were found in their blood. In the last group irradiated quinine brought about only a temporary reduction of the temperature whereas in the true malaria cases the results of treatment were very promising. As a rule the first dose prevents further paroxysms except in malignant tertian malaria with daily paroxysms. In the latter case febrile symptoms were sometimes observed two or three days after treatment. As regards the parasites these disappeared in 2-3 days in benign tertian malaria while the gametes of *P. falciparum* disappeared after a fortnight. The most important result of this treatment is thus the rapid cessation of attacks of fever and the absence of relapses in patients kept under observation up to eighteen months after a course of treatment.

C. A. Hoare

GOTTFRIED S. P. & LEVINE A. C. Liver Function Studies on Soldiers under Prolonged Atabrine Administration. *J Lab & Clin Med* 1945 Oct v 30 No 10 853-5 [17 refs.]

Fifty Negro soldiers who had been taking atabrine 0.1 gm. six days a week for 18 months were examined. None had had clinical malaria, syphilis, scrub typhus or jaundice. The tests employed were icterus index, urine urobilinogen, fibrinogen, serum cholesterol partition and the oral hippuric acid test. Where the total serum cholesterol values were high, total serum lipid determinations were made. As a check on the fibrinogen results this determination was also performed on 50 other soldiers who had been taking atabrine for only from one to three months.

Several months later bromsulphalein, cephalin flocculation and galactose tolerance tests were performed on 50 more soldiers who had also been taking atabrine for from 20 to 24 months. As a control of the sensitivity of the cephalin flocculation test determinations were performed on 25 soldiers who had been taking atabrine from one to three months.

At a still later date 25 additional bromsulphalein tests were done on soldiers who had been taking atabrine for 30 months.

Plasma fibrinogen was determined colorimetrically. Icterus index was determined by the method of MEULENBACHT (*Deut Arch f Klin Med* 1920 v 132 285), urine urobilinogen by SPARKMAN's method (*Arch Intern Med* 1939 v 63 856), oral hippuric acid test by QUICK's method as modified by KRAUS and DULKIN (*J Lab & Clin Med* 1941 v 26 729 & 1078). Total serum cholesterol was measured colorimetrically and free cholesterol by the method of SCHOENHEIMER and SPERRY (*J Biol Chem* 1934 v 106 745). The total lipid content was measured gravimetrically. The bromsulphalein test was done by injecting 2 mgm. per kgm. of body weight and by measuring the retention at the end of 18 minutes. The cephalin flocculation test was done by HANGER's method (*J Clin. Invest.* 1939 v 18 261) and the galactose tolerance test by the method of JANNEY and ISAACSON (*J Amer Med Ass* 1918 v 70 1131).

Of all the hepatic function tests employed only the hippuric acid test gave results indicative of hepatic dysfunction and then in only very few cases. This by itself was not significant. The conclusion is that no subclinical liver damage could be detected among the soldiers studied.

Norman White

*J AMER MED ASS* 1945 Dec. 15 v 129 No 16 1091-3 Untoward Reactions attributable to Atabrine.

This report represents the views of a considerable number of U.S. Army medical experts on cutaneous reactions that have resulted from the administration of suppressive atabrine, notably the atypical lichen planus syndrome.

The condition was observed in the latter half of 1943 in soldiers who had been evacuated from New Guinea and adjacent islands. The syndrome has been most commonly seen in this area and in Assam and North Burma elsewhere only few cases have occurred. The incidence of these cutaneous lesions has been low even in New Guinea, and has not constituted an important handicap from the military point of view. Cutaneous reactions have been more frequent in persons who have taken suppressive atabrine in larger doses than the recommended amount 0.7 gm. per week.

It is suggested that the cutaneous reactions attributed to atabrine should be grouped under the heading "atabrine dermatitis complex" and be classified as: (a) lichenoid dermatitis (b) lichenoid and eczematoid dermatitis (c) eczematoid dermatitis (d) exfoliative dermatitis secondary to (a) (b) or (c).

Usually the disease is characterized by localized violaceous or erythematous eczematoid plaques on the dorsal surface of hands or feet, side of the neck, or elsewhere followed by generalization of the lesions with subsequent appearance of lichenoid plaques and mucous membrane lesions. A characteristic eczematoid dermatitis has also occurred in persons taking suppressive atabrine. There are bilateral, symmetrical, violaceous-tinged, vesicular eczematoid and oozing plaques on hands, feet, legs and sometimes other parts of the body. Secondary pyogenic infection is common.

The treatment of these conditions depends on early recognition of their nature and discontinuation of atabrine. Whenever possible such cases should be seen by a competent dermatologist and every effort should be made to rule out other aetiological factors. The very much higher incidence in New Guinea and adjacent islands, Assam and North Burma than elsewhere suggests that climatic or other geographical factors play a rôle in causation. Various forms of cutaneous trauma may contribute to the onset and localization of lesions.

An adequate summary of this important paper is not possible. The general statement at the end of the report "for the information and guidance of all concerned," is as follows —

"(1) The military value of atabrine in suppressing vivax malaria and curing falciparum malaria far outweighs untoward effects which have been attributed with reason to the use of the drug.

"(2) Suppressive doses of atabrine greater than 0.7 gm. per week should not be employed routinely. This amount has been shown to provide adequate protection against clinical attacks of malaria provided atabrine discipline is strictly enforced. In clinical treatment of malarial attacks with atabrine, routine dosage should not exceed 2.8 gm. in seven days.

"(3) Atabrine suppressive medication should be discontinued promptly and atabrine should not be given for clinical treatment when persons develop atypical lichen planus, unexplained chronic eczematoid dermatoses, unexplained toxic erythematous eruptions, exfoliative dermatitis, severe leukopenia, agranulocytosis and aplastic anemia, acute hepatitis (not including disturbances believed to be due to malaria) or toxic psychoses which can be reasonably attributed to atabrine after careful clinical study.

"(4) It should be remembered that drugs other than atabrine such as the sulfonamides and arsenicals, may be harmful to persons with the conditions mentioned.

"(5) Caution should be exercised in attributing disease conditions to atabrine until careful and complete studies have been made over a period of time to establish such relationship. Because of the widespread use of atabrine, its administration inevitably coincides with many diseases with which the drug has no connection. Even if a connection is established between atabrine and a given untoward effect, its significance relative to the military value of atabrine requires evaluation. It should be remembered that, since the use of atabrine became widespread, clinical attacks of falciparum malaria have been almost eliminated and deaths from

malaria have been extremely rare There is no question of the general superiority of atabrine over quinine both for suppression and for clinical treatment

Norman White  
Bull U.S. Army Med

WHITEHILL R. Skin Sensitivity due to Atabrine Bull U.S. Army Med Dept 1945 Dec 4 No 6 724-5

An Army nurse had occasional contact with atabrine [mepacrine] during 1939 1940 and 1941 and from October 1942 she had frequent contact with it every day She was admitted to hospital on 6th November 1943 with an itching rash on the eyelids. There was no family or personal history of allergy or of skin disease She had used various cosmetics and a hair lotion for dan druff The rash appeared 3½ weeks before her admission as a small scaly lesion on the lids of the right eye on the left eyelids next day and a few days later a small patch appeared behind the right ear The patches slowly enlarged and the itching interfered with sleep.

On admission the skin of the eyelids and behind the right ear showed a scaly erythematous rash and the conjunctivae were somewhat injected. Patch tests with the cosmetics and other substances with which she had had contact gave negative results. She was treated with Burrow's solution (Liquor Alumini Acetas) diluted 1/20 and on November 20th she returned to duty in the medical ward.

On 24th November the rash reappeared on her eyelids as an erythema with tiny vesicles Patch tests were made with various drugs and all were negative except the test with atabrine which produced a 3+ reaction with erythema and a few vesicles itching beginning within 12 hours. The rash gradually faded and disappeared in two weeks. The nurse was transferred to a surgical ward and had no further attacks

J F Corson

NELSON L. M. Dermatitis from Atabrine Bull U.S. Army Med Dept 1945 Dec 4 No. 6 725-7

Two cases of dermatitis in American soldiers apparently caused by atabrine are reported. The first patient developed a pruritic dermatitis about 2 months after he began to take suppressive doses (0.4 gm. a week in divided doses) of atabrine in the summer of 1943 the rash appeared first on his wrists and afterwards in spots all over his body When he stopped taking atabrine in the autumn of 1943 the rash disappeared but returned in the following May 11 days after he again began to take atabrine He was now seen by the author who observed that he had violaceous macular lesions about 5 mm. in diameter on the front of his wrists and upper part of the palms of his hands He stopped taking atabrine and the pruritus disappeared in 3 days For diagnostic purposes he again took 0.1 gm. of atabrine on June 2 3 and 4 and the same pruritic rash reappeared on June 4 A patch test of atabrine applied on June 5 was negative on June 7

The second patient took atabrine in suppressive doses (0.4 gm. a week in divided doses) during the summer of 1943 until his admission to hospital on October 15 In the last week of September he developed dermatitis on the left ankle and right wrist this was treated with sulphadiazine ointment but the rash appeared on the eyelids and ears and after admission bullae appeared on the arms and legs and a generalized exfoliative dermatitis finally developed. He lost part of his hair and deep depressions formed on the finger nails. He slowly recovered under local treatment in hospital and was discharged on 5th February 1944

He had minor local attacks of dermatitis between February and April and on April 14 he again began to take atabrine as before three days later his



eyes and ears became swollen and he was admitted to hospital and was seen by the author. He then had generalized dermatitis—exudative on the groins, genitalia, popliteal and cubital spaces and ears, oedema of the face, especially the eyelids, follicular vesicles on the arms and thighs and vesiculo-papules over the rest of the body. He gradually recovered under local treatment.

A patch test of atabrine was negative at 48 hours and positive (papulo-vesicular rash) at 60 hours. A patch test with 5 per cent. sulphadiazine in lanoline and petrolatum was positive (vesicles) at 48 hours while a patch test with powdered quinine was negative at 48 hours. A patch test with atabrine done on 8 control persons was negative.

Few cases of dermatitis due to atabrine have been reported. The author saw another case, in a medical officer in 1943 and refers to two cases reported by NOOJIN and CALLAWAY (*North Carolina Med. J.*, 1942, v 3 239).

J. F. Corson.

CEOPRA, R. N. & CHOPRA, I. C. Individual Variations in the Absorption of Drugs from the Gastro-Intestinal Tract. *Indian Med. Gaz.*, 1945 May v 80 No. 5 267-71.

A description of the physiology of the various parts of the alimentary tract precedes a discussion of the factors responsible for remarkable individual variations observed in the absorption of drugs, not least of antimalarial drugs. The absorption of drugs is modified in inflammatory conditions of the mucous membrane of the gut, and by hypoacidity which commonly characterizes chronic dysentery and other infections. The rapid passage of meals through the intestinal tract in dysenteries, liver diseases and other conditions hinders absorption. Five illustrative cases are described in which failure of malaria infected patients to respond to the administration of antimalarial drugs was explained by much delayed absorption, as revealed by urine examination.

Norman White

BOYD, M. F. & KITCHEN, S. F. On the Employment of Quinacrine Hydrochloride in the Prevention of Malaria Infections. *Amer. J. Trop. Med.* 1945, July v 25 No. 4 307-14.

The experiments described were designed to assess the protection afforded by mepacrine against malaria infection. Patients were inoculated by the application of various lots of insectary reared *A. quadrimaculatus* experimentally infected with either *P. vivax* or *P. falciparum*. The patients were white adult males presumably susceptible to infection. The experiments which are described in detail, indicate that the administration of mepacrine, 0.1 gm. six days a week, begun a week before and continued throughout the period of exposure gave complete protection against *P. falciparum* but failed to protect against *P. vivax*. In some instances the small dose of 0.1 gm. on two discontinuous days a week appeared to protect against *P. falciparum* and in one case though parasites appeared in the blood, there was no clinical malaria. Even if the period of administration of 0.1 gm. six times a week be commenced two weeks before and continued to two weeks after the period of exposure to infection *P. vivax* later becomes clinically active after protracted incubation periods.

Norman White

LEWIS, R. A. & KIRBY, F. W. Suppression as an Adjunct to the Therapy of Malaria in Non-Malarial Areas. *Bull. Johns Hopkins Hosp.* 1945 Sept., v 77 No. 3 211-17.

These observations concern a group of 63 members of the Medical Detachment of a General Hospital, who were suffering from *P. vivax* infections causing

frequent early relapses. The observations were made in an area in which there was no possibility of natural reinfection. The clinical treatment of the acute attack most frequently employed was 2.8 gm. of atabrine during a seven day period. It was found that if the clinical treatment of the recurrence was followed by the administration of 0.1 gm. atabrine daily for two months the interval between relapses was increased from less than six weeks to more than four months and the percentage of relapses was reduced from 80 to less than 50. The less frequent periods of hospitalization resulting from this suppressive treatment resulted in improved morale. Many of the men so treated gained weight notably so in the case of men in whom repeated attacks of malaria and weight loss had been associated. In most cases headache and weakness cleared up but there were exceptions.

Norman White

BUXTON P. A. Experiments with DDT in Solutions and Emulsions against Mosquito Larvae in West Africa. *Bull. Entom. Res.* 1945 Sept. v 36 Pt. 2, 165-75.

The experiments described were carried out near Takoradi Gold Coast and were designed to assess the relative effectiveness of different preparations containing DDT as larvicides. These were tested against *A. funestus* larvae in ditches about two feet wide separated from each other by ridges some six feet wide in a vegetable garden. These provided good opportunities for repetition and measurement of dose of larvicide per unit area.

An emulsion was made by dissolving DDT in two volumes of lubricating oil (Pool Grade 3) and one volume of Armo A.S.X. an oil-soluble emulsifier. The DDT content was 5 per cent. by weight of pure DDT. Diluted to 1:10 this makes a very lasting emulsion.

A dieselene solution was made by dissolving a commercial DDT 60 per cent. pure in a locally available dieselene generally a 5 per cent. concentration of pure DDT was used but for putting on very small doses a 0.5 per cent. concentration was suitable.

Preliminary experiments showed that neither kerosene nor dieselene without DDT were larvicidal in doses up to 0.5 cc. per square yard.

The dieselene solution was more effective than the emulsion as is shown in the following table —

Dose cc. 5 per cent. pure DDT per sq. yd.	Emulsion		Dieselene	
	Immediate (kill %)	Lasting (days)	Immediate (kill %)	Lasting (days)
0.01	—	—	100	1-2
0.02	Nil	Nil	80-100	2-3
0.10	Over 80	1-2	100	4
0.50	95-100	7-10	100	6 (several weeks partial)

In shallow water DDT seems to dissolve from oil into water so as to make a larvicidal solution.

The larvicidal effect passes off in a few days even when a high dose (0.10 cc. of 5 per cent. DDT per square yard) has been applied on stagnant water. It is not known what happens to the DDT. A heavy dose (0.5 cc.) after a period of complete kill exercises partial irregular larvicidal effect for as much as four weeks. This action is not explained.

Creatures that prey on mosquito larvae were not destroyed in these experiments. Norman White

CAMBOURNAC, F. J. C. & SIMÕES, J. M. P. Nota sobre alguns ensaios realizados com Neocid e 7013 Geigy contra as larvas de *Anopheles* [Experiments with Neocid and 7013 Geigy as *Anopheles* Larvicides.] *An. Inst. Med. Trop. Lisbon*, 1944 Dec. v 1 No 2 333-32.

Neocid and 7013 are substances allied to DDT (dichlor-diphenyl-trichlor ethane). Neocid is said to have the composition trichlor-4, 4-dichlor diphenylmethane mixed with an inert powder in the proportion of 5 per cent. The composition of 7013 Geigy is not given. The larvicidal action of both these substances was tested against the larvae of *A. maculipennis atroparvus* under natural conditions. They were applied as 1 per cent. mixtures with road dust and in liquid suspension. The amounts of Neocid in suspension were 0.05 gm. and 0.2 gm. per square metre and with dust 0.1 gm. per square metre. The amounts of 7013 used were 0.2 gm. per square metre in suspensions and 0.1 gm. per square metre in dust. On occasion larvae were totally eliminated, but the results were not consistent. Sometimes the smallest larvae appeared most resistant at other times larvae of the later stages. The larvicidal action was of short duration. Norman White

WERTZ, R. Senior. House Spraying with D.D.T. and with Pyrethrum Extract compared. First Results. *J. Malaria Inst. of India*, 1945 June v 6 No. 1 83-80.

The locality selected for this experiment is in the hyperendemic Jaypore Hills the malaria conditions in this area have been previously described by the author (this *Bulletin* 1937, v 34, 627). The three villages referred to in this paper still have very high spleen rates: Chatikona 98.0 Jimidiguda 87.8 and Bariguda 92.7 per cent. Jimidiguda, a small village of 48 houses was sprayed with a 5 per cent. solution of DDT in grade III kerosene applied with a De Vilbiss paint gun served by a Kaper hand pressure sprayer at the rate of 1 qt. per 1 000 square feet of wall surface. Care was taken to wet all the wall surfaces including outside verandahs and the roofs as far as accessible. Chatikona was sprayed with pyrethrum insecticide. Bariguda was an untreated control. The author's conclusions are as follows—

"(i) D.D.T. at the rate of 1 qt. 5 per cent. solution per 1 000 sq. ft. will prevent infection in the *farvacilis*-group in a hyperendemic area, in the cold weather of Southern India, for eight weeks. It acts by reducing density as well as longevity.

"(ii) Pyrethrum spraying, 6 days each week, reduces density and longevity sufficiently to inhibit gland infections. The density reduction is much less than with D.D.T. This is probably due to a certain proportion of the house population leaving before the morning pyrethrum spraying, whereas with D.D.T. it is believed that any specimen which has rested after feeding on a still active treated surface must die.

"(iii) Pyrethrum spraying twice a week has no effective result either on density or on infectivity. As a method of protecting a population exposed to the *farvacilis*-group it is useless.

"(iv) Assuming the cost of D.D.T. as stated to be correct (Rs. 3 per lb.), over the two months December to February a period of heavy though not of maximal transmission, D.D.T. is 20 to 25 times cheaper per capita per week than pyrethrum."

Norman White

COLLIGNON E La campagne antipaludique de 1944 dans le département d'Alger [The Antimalaria Campaign in the Department of Algiers in 1944] Arch Inst Pasteur d'Algérie 1945 June v 23 No 2 98-110

As in 1943 the malaria campaign in 1944 concentrated on the protection of military forces stationed in the Algiers Department. The antimalaria services of the British and United States armies and of the local government were each responsible for a delimited area. This arrangement only related to measures against the anopheline vector drug prophylaxis being in the charge of each authority as concerned its own personnel.

It was a difficult year for the departmental service. The shortage of anti-malarial drugs prevented their use for prophylaxis. Transport difficulties and the difficulty of recruiting labour of a reliable type were obstacles to the satisfactory execution of antilarval measures. Nevertheless the malarial situation was not unsatisfactory there were no important epidemic manifestations and climatic conditions limited anopheline breeding places. Indices of infection were if anything somewhat lower than in the two preceding years.

Norman White

INCKE I with PARENT M. Un essai de lutte antimalarienne spécifique à Stanleyville [Control of Malaria in Stanleyville by Species Sanitation.] Reprinted from Bull Ass des Ingénieurs de la Faculté Technique du Haut Congo 1944 Oct. No 8 23 pp 7 graphs & 1 map [15 reils]

*Anopheles gambiae* is by far the most important vector of malaria in Stanleyville and from 1935 to 1940 all efforts were concentrated on the control of this species. This paper describes the results achieved. *A. mouchelet*, *A. nili* and *A. funestus* are also vectors of malaria but their relative infrequency makes them comparatively unimportant. Thus of more than 50 000 identified anophelines captured in dwellings *A. gambiae* formed 85.5 per cent. *A. nili* 8.7 *A. mouchelet* 5.6 and *A. funestus* 0.18 per cent. Of 18 396 anopheline breeding places 93.5 per cent harboured larvae of *A. gambiae*. Temporary breeding places of *A. gambiae* have necessitated close and constant supervision. oiling or filling was used in their treatment. Permanent breeding places have necessitated drainage works. Creeks and inlets from rivers have presented great difficulties: some success has been achieved by providing shade for breeding places with species of *Cassia*. *C. alata* which flourishes in damp situations.

In 1938 oiling which previously had been done at 10-day intervals was carried out weekly thereafter there was a marked diminution in the anopheline infestation of houses. But the improvement was not reflected in any diminution in the parasite rate of children between 5 and 10 years of age. this rate was 95.7 in 1940. The spleen rates of children of the same age were much lower than those reported for Stanleyville by SCHWETZ in 1931. he reported a rate of 94.8 as compared with 37 in 1940 but the fall preceded the antilarval work reported in this paper.

Of the positive blood slides from children aged 5 to 10 *P. falciparum* was found in 94.6 per cent. *P. malariae* in 22 per cent. and *P. vivax* in 4.5 per cent. *Anopheles* dissected numbered 36 826. The sporozoite index of 30 780 *A. gambiae* was 6.49 of 3 589 *A. nili* 4.3 of 2 062 *A. mouchelet* 4.4 and of 375 *A. funestus* 6.6.

Norman White

REV PALUDISME ET M&D TROP 1945 Dec. 15 v 3 No 21 167-76. La lutte contre le paludisme dans la France d'Outre-Mer [Malaria Control in French Overseas Territories.]

[April, 1946]

FELTON H. L. BARNES R. C. & WILSON A. Malaria Control in a Non-endemic Area. *J National Malaria Soc.* Tallahassee Fla. 1945 Sept. v 4 No. 3 201-8. [16 refs.]

The return of service personnel and the introduction of prisoners of war from many parts of the world, infected with malaria involves risks not limited to those parts of the United States in which malaria is endemic at the present time. This paper describes the activities of a sub-office of Malaria Control in War Areas with headquarters in New York that is responsible in collaboration with local authorities for the execution of preventive measures around military installations in the New England States New York New Jersey Pennsylvania and Delaware. Mobile malaria control units have been established at strategic places. Each unit consists of a station wagon and a 1½-ton truck which carries material for entomological surveys and inspections larvicidal operations minor drainage clearing and cleaning and spray-killing adult mosquitoes an engineer or entomologist is in charge and is accompanied by the necessary semi-skilled assistants. Surveys are made around concentrations of prisoners of war and service personnel and assistance is given to local agencies making such surveys in non-military areas. Mosquito control measures are carried out wherever human carriers and the mosquito vector are concentrated. In addition demonstrations have been given to district and local public health officials and laboratory workers have been trained in the recognition of malaria parasites in thick films.

During 1943 and 1944 57 areas were surveyed in all of these north-eastern States except Vermont. *A. quadrimaculatus* was present in 32 of these 57 areas adults were found in all the States except New Hampshire where however larvae of this species were taken. In nine localities *A. quadrimaculatus* densities were high. Maximum *A. quadrimaculatus* counts for single catching-station inspections were as high as 500 in Rhode Island 325 in Delaware 200 in Massachusetts 150 in New Jersey and 100 in New York. It would seem that high densities of *A. quadrimaculatus* may be found in all of the north-eastern States except Maine Vermont and New Hampshire.

Norman White

KIRK, C. C. & SPARKMAN R. E. A Review of Equipment used in applying Malaria Control Measures on Impounded Waters in the Tennessee Valley. *J National Malaria Soc.* Tallahassee Fla. 1945 Sept. v 4 No. 3, 209-22, 9 figs.

This is a brief description of machines and equipment of many kinds that have been used in the comprehensive programme of malaria control of the Tennessee Valley Authority during all stages of construction of impounded waters. Tractor-drawn and self-propelled machines used for clearing the land to be submerged and for shore-line maintenance a floating underwater weed cutter and two types of spray equipment for applying insecticidal sprays are among the equipment described in a paper which does not lend itself to summary.

Norman White

KRUEK, C. W. & GARTRELL, F. E. The Use of House Mosquito-Proofing as an Emergency Malaria Control Measure in the Kentucky Reservoir. *J National Malaria Soc.* Tallahassee, Fla. 1945 June v 4 No. 2, 133-49 2 figs.

PARAENSE L. Aspectos parasitários observados no local inoculado com esporozoítos de *Plasmodium gallinaceum* (Nota preliminar) [Parasitologia.] Mem Inst Oswaldo Cruz 1943 June v 33 No 3 353-9  
1 coloured pl English summary

The paper reports the results of an investigation into the development of sporozoites of *P. gallinaceum* when injected by mosquito bite or by syringe into the skin of chicks. The skin at the site of injection was removed at varying intervals and pinned out on a board with the subcutaneous surface uppermost. Scrapings were then made of the dermis and with the material thus obtained films were made. These were stained with Giemsa stain and searched for possible developmental forms of the malarial parasite. Films made from skin 6 to 12 hours after injection showed many elongate bodies with eight or more chromatin granules. They were considered to be evolutionary forms of sporozoites. At the 18, 24, 60 and 84-hour periods the films showed small intracellular oval bodies with one or two chromatin masses. After the 84-hour period parasites appear in the blood following which after 1, 24 and 48 hours smears from the injection sites reveal numerous erythrocytic schizonts within large cells. The paper is illustrated by a coloured plate depicting some of the developmental forms encountered.

SEELER A. O. MALANGA C & PIERSON J. Effect of Streptomycin on Avian Malaria. *Proc Soc Exper Biol & Med* 1945 June v 59 No 2 291-2  
C M Wenyon

The authors have tested the action of streptomycin on three species of avian malarial parasite (*P. cathemerium*, *P. lophurae* and *P. gallinaceum*) in Leghorn chicks. The infections were produced by intravenous inoculation of infected blood, and, in the case of *P. gallinaceum* of sporozoites also. Treatment was commenced within an hour of inoculation by intramuscular injection of the antibiotic every three hours during five days (three days in the case of the sporozoite induced infection). The birds were in groups of five and the dose for each group varied from 25 000 to 400 000 units per kilogram of body weight per day. The effect of the drug if any was estimated by parasite counts made on the fifth day (ninth day in the sporozoite-infected birds). In the blood-inoculated birds the infections developed as in the controls but in those inoculated with sporozoites the percentage of infected cells in the blood varied from 40.8 to 17.7 according as the doses of streptomycin varied as indicated above. In 10 control chicks the percentage of infected cells was 35.1. The results indicate that streptomycin has no suppressive action on the blood inoculated infections but has a slight action on those induced by sporozoite inoculation.

ROSTORFER H. H. & RIGDON R. H. Anoxia in Malaria. An Experimental Study on Ducks. *J Lab & Clin Med* 1945 Oct. v 30 No 10 860-66  
4 figs. C M Wenyon

In previous papers the second author has shown reason for supposing that anoxia plays an important part in deaths from *P. falciparum*, *P. knowlesi* and *P. lophurae* infections [this *Bulletin* 1943 v 40 118 and 436 1945 v 42 540]. Recently with VARNADAE (*Amer J Trop Med* to be published) he has shown that transfusion of red cells will prolong the course of the infection in ducks but will not prevent ultimate death. In the present paper an account is given of experiments in which chicks and ducks infected with *P. lophurae* were exposed to reduced oxygen tension. This was accomplished by keeping

them in a special chamber in which atmospheric pressure could be reduced to represent the conditions of altitudes up to 20 000 feet. The rate of "ascent" was 1 600 feet per minute during the first 12 minutes followed by 600 feet per minute. It was found that both normal and infected chicks and ducks succumbed to the reduced oxygen tension, but that the infected birds did so before the normal birds. The normal birds developed a polycythaemia of 4 million red cells in comparison with a normal of 2.5 million. In ducks this level was reached in three days.

In another experiment a comparison was made of four infected ducks kept at normal atmospheric pressure and four at the reduced pressure of 20 000 feet. The total red cell count showed an increase on the second day and a subsequent fall, in both groups. The fall is however more rapid in the normal-atmosphere group while the total number of parasitized cells is one-third greater in the reduced pressure group. The total number of unparasitized cells decreases rapidly in both groups so that, ultimately the complete loss of these cells seems evident. The formation of young cells is more rapid in birds kept at high altitude. The increase in number of the new cells does not prevent the rapid disappearance of the old cells. The rate of disappearance of adult cells is the same in both groups though the total parasite count is higher in the reduced-atmosphere group. Observations were also carried out on six ducks two of which were kept at normal atmospheric pressure and four at reduced pressure. Of the four two were removed from the chamber after five days. The results were very much the same as in the previous experiment. Of the two removed after five days one recovered and its rate of recovery was approximately the same as that of one of the two kept at a normal pressure which also recovered.

The experiments indicate that birds with a mild infection do not tolerate severe anoxia such as occurs at high altitudes. They first show the effects of anaemic anoxia before the infection has reached the stage at which malarial symptoms would become evident. The symptoms of anoxia in infected and uninfected birds are the same with the difference that they appear at a lower altitude and after a shorter exposure in the former group. It appears that the decrease in resistance to anoxia in infected birds is the result of the failure of the oxygen transporting system to meet reduced oxygen pressure. The high total parasite count in infected birds at high altitudes is a result of the induced polycythaemia and the greater opportunity the parasites have of infecting red cells.

The authors conclude that the data presented in their paper lend support to the view that anoxia plays an important rôle in the mechanism of death from acute malarial infections.

C. M. Wenyon.

RIGDON, R. H. & RUDISELL, H. JR. Effect of Radiation on Malaria. An Experimental Study in the Chick and Duck. *Proc Soc Exper Biol & Med.* 1945 June v 59 No. 2, 167-70 2 figs.

One of the authors (H. R.) having shown that splenomegaly resulting from chronic malaria was reduced, with corresponding improvement in health by treatment with Roentgen irradiation it was considered of interest to investigate the effect of irradiation on more easily controlled malarial infections. Those of *P. lophurae* in chicks and ducks were selected. In the first place citrated infected blood was exposed in Petri dishes to varying amounts of irradiation, and was then inoculated intravenously to chicks and ducks. It was found that the intensity of infection produced in a given time decreased with the amount of irradiation till finally an amount was reached which rendered the blood entirely non-infective. When infected chicks were exposed to the rays there was a reduction in the intensity of the infection, the greatest reduction being in the

chicks which had been exposed to the greatest amount of irradiation. The effect of radium bromide was tested by mixing a solution of this substance with citrated infected blood in Petri dishes or by inoculating the solution intravenously to infected chicks and ducks. In neither case was there evidence of any lethal action of the drug on the parasites though in the case of the *in vivo* test the amount administered was sufficient to cause severe tissue degeneration. In the Roentgen ray experiments as the amount of irradiation needed to bring about a significant reduction of the infection was very near the dose lethal for the chicks and ducks it would seem that this type of therapy for malaria would be impracticable unless other malarial parasites proved much more susceptible. Similar experiments with *P. gallinaceum* have been described by BENNISON and COATNEY [this *Bulletin* 1945 v 42 623] C M Wenyon

- I. FREUND J SOMMER Harriet E. & WALTER Annabel W Immunization against Malaria Vaccination of Ducks with Killed Parasites Incorporated with Adjuvants. *Science* 1945 Aug 24 200-202.
- II. — THOMSON K. J SOMMER, Harriet E WALTER Annabel W & SCHENCKEN Edna L Immunization of Rhesus Monkeys against Malarial Infection (*P. knowlesi*) with Killed Parasites and Adjuvants. *Ibid* 202-4 [Refs in footnotes.]

Experiments by various observers have shown that antibody production against certain antigens is increased and made to last longer if the antigens injected are combined with a lanoline like substance (Falba) and paraffin oil with or without killed tubercle bacilli [see *Bulletin of Hygiene* 1945 v 20 585]. In the papers under review experiments are described in which this procedure was applied in attempts to immunize young ducks against *Plasmodium lophurae* and *rhesus* monkeys against *P. knowlesi* both of which usually produce fatal infections.

i. In the first paper the experiments with ducks are considered. Heavily parasitized red cells were suspended in salt solution containing 0.1 per cent formaldehyde and kept at a temperature of 4°C. overnight. The cells were then washed three times with saline and mixed with Falba and paraffin oil. The ducks to be protected received two injections of this mixture together with killed tubercle bacilli and one injection of the mixture without tubercle bacilli a period of one month intervening between the injections. A month after the last injection of antigen in each of two experiments four immunized and four control ducks received approximately one billion parasites intravenously. The blood examinations carried out clearly indicated that the intensity of infection in the immunized ducks was very much lower than in the controls. Thus in the first experiment none of the immunized ducks showed more than an average of 7.6 parasites per 100 red cells while none of the controls showed less than 54. Two of the controls died from their malaria infection. One of the immunized ducks also died the cause of death being generalized peritonitis. It is clear that the immunized ducks had acquired a considerable resistance to subsequent infection with *P. lophurae*.

ii. In the second paper are discussed similar experiments with *rhesus* monkeys and *Plasmodium knowlesi*. The antigen was prepared from heavily infected blood as described above and monkeys received two or three subcutaneous injections of this antigen with killed tubercle bacilli. When injected intravenously with infected blood 14 control monkeys rapidly became infected. Of these four died of malaria nine most if not all of which would have died, were killed in order to recover parasites for vaccine production while one survived. Of similarly treated immunized monkeys one failed to show parasites at any time in thin smears while 6 developed infections of 1 to 10 parasites per 100



red cells. These subsequently disappeared. It is concluded that the method of immunization modifies parasitaemia and prevents fatal infection with *P. knowlesi* in rhesus monkeys. C. M. Wenyon

### TRYPANOSOMIASIS.

CAURET P. Différences morphologiques chez deux souches de *Trypanosoma gambiense* déterminant des maladies expérimentales différentes. [Morphological Differences between Two Strains of *Trypanosoma gambiense* causing Different Experimental Infections.] Bull. Soc. Path. Exot. 1944 v 37 Nos 9/10 285-90 2 figs. [16 refs.]

The author measured the trypanosomes of two laboratory strains of *Trypanosoma gambiense* using stained thin blood films and a camera lucida. One strain called the Antwerp strain produced acute infections in mice and rats, while the other called the Yaounde strain [Cameroons] caused chronic and irregular infections and sometimes produced paralysis in mice. The latter strain has been the subject of previous observations (see ROUBAUD & PROVOST this Bulletin 1939 v 36 746 1942 v 39 234 STÉFANOPOULO & ETÉVÉ *ibid.* 1945 v 42, 258).

The measurements of the two strains are shown in tables and curves. The trypanosomes of the Antwerp strain were in general shorter than those of the Yaounde strain, owing chiefly to differences in the length of the free flagellum. In the Antwerp strain the total length of the trypanosomes varied from 18 to 30  $\mu$  (average 24.5  $\mu$ ) in the guinea pig and from 16 to 28  $\mu$  (average 22.9  $\mu$ ) in the rat, while the corresponding figures for the Yaounde strain were 20 to 34  $\mu$  (average 29  $\mu$ ) and 20 to 34  $\mu$  (average 27.6  $\mu$ ).

These differences between the two strains were maintained through many passages in animals during six months and the strains could readily be distinguished in thin blood films on simple microscopic examination.

In accordance with the views of LÄVIER (this Bulletin 1944 v 41 368) the author thinks that the morphological differences may be associated with differences in the rates of multiplication of the trypanosomes, the longest ("oldest") forms tending to be eliminated among the rapidly dividing trypanosomes of the Antwerp strain. J. F. CORSON.

JACKSON C. H. N. Comparative Studies of the Habitat Requirements of Tsetse Fly Species. J. Animal Ecology 1945 May v 14 No. 1 46-51

In an attempt to discover why different species of *Glossina* are found in different types of country *G. morsitans* and *G. palpalis* were introduced into territory where *G. swynnertoni* normally occurs. This was done by allowing pupae brought from indigenous areas to hatch in the new habitat.

The *morsitans* were able to produce a second generation in the new environment, but were physiologically inferior to *morsitans* in a normal habitat, being smaller and containing less reserve fat. It is suggested, however, that this species would die out not so much for physiological reasons but because the predominant *swynnertoni* males would impregnate the *morsitans* females such females are either barren or produce few mostly sterile offspring.

*G. palpalis* did not produce a second generation under the new conditions although a seasonal stream (containing water at the time of the experiment) was in the vicinity.

Laboratory experiments to elucidate these results are described, and future work is suggested. The ability of each species to colonize a particular type of

country appears to be related more to its behaviour (frequency of feeding, choice of resting place) than to its straightforward physiological reactions to climatic conditions

Kenneth Mellanby

GASCHEN H. La répartition des tsé-tsés en fonction du climat. [The Distribution of Tsetse Flies in relation to Climate] *Bull. Soc. Path. Exot.* 1944 v 37 Nos. 5/6 172-5.

—— L'utilité du climogramme pour l'étude de la biologie des tsé-tsés. [The "Climogram" in the Study of Biology of Tsetse Flies.] *Ibid.* 176-80 1 fig

Details are given of how the limiting conditions of temperature and humidity under which *Glossina tachinoides*, *G. morsitans* and *G. palpalis* occur can be determined and expressed graphically, and the way in which these climatic conditions are related to other factors such as vegetation in the ecology of the tsetse is discussed. The ideal climatic zone for *G. tachinoides* is very much larger than that for *G. palpalis* which is much more susceptible to adverse conditions such as high temperature and low relative humidity. *G. morsitans* is intermediate between the other species in the range of its climatic requirements

K. Mellanby

GASCHEN H. Variations saisonnières des tsé-tsés [Seasonal Variations of Tsetse Flies.] *Bull. Soc. Path. Exot.* 1944 v 37 Nos. 7/8 250-53 2 figs

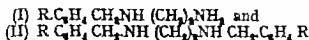
The relative abundance of *Glossina palpalis* and *G. tachinoides* at different seasons of the year is related to the changes in the temperature and humidity at the different seasons. The author considers that there is a close correlation between the abundance of *G. palpalis* and the moisture of the air from March to June when the relative humidity is rising from 40 to 80 per cent, the fly population increases greatly. Later in the year the fly catches are smaller owing to the wide dispersal of the flies from their dry weather foci. With the return of hot dry weather the flies are reduced in numbers and the extent over which the species can range is also restricted. *G. tachinoides* being much less susceptible to desiccation is less closely dependent on a favourable atmospheric humidity and variations in the density of *G. tachinoides* population are not correlated in the same way

Kenneth Mellanby

NEEL, R. Sur un cas de trypanosomiase africaine au début, avec complications rénales observé chez un Européen au Soudan. [An Early Case of Sleeping Sickness with Renal Complications, in a European.] *Bull. Soc. Path. Exot.* 1944 v 37 Nos. 3/4 100-107 3 figs.

LWOFF M. Mme. BOVET D. & FUNKE A. Activité *in vitro* sur les trypanosomides de quelques dérivés de l'éthylène diamine. [Action of various Derivatives of Ethylenediamine on Trypanosomidae *in vitro*] *Bull. Soc. Path. Exot.* 1944 v 37 Nos. 7/8 229-36.

It had previously been shown that a number of derivatives of ethylenediamine possess therapeutic properties against *T. brucei* infections in mice (FUNKE, BOVET and MONTEZIN this Bulletin 1944 v 41 734). These were of the types —



where R and R are various hydrocarbon radicles. The present studies are intended to show whether such compounds exhibit any activity against artificial cultures of flagellates. The organism chosen for the tests was *Strigomonas*

*oncopelti* a non-pathogenic parasite of Hemiptera and plants a peptone-saline culture medium being used adjusted to pH 7.0. One compound was tested also against *Leishmania tropica* *L. donovani* and *Trypanosoma cruzi* in a semi-solid blood-containing culture medium. The experiments were conducted at 26-28°C. in drug-concentrations of 1/1 000 1/2,000 1/5 000 and 1/10 000.

Eighteen compounds were tested results being presented in a Table. The authors' conclusions are that the degree of correspondence between the findings *in vitro* and those previously obtained *in vivo* varied in different chemical groups as follows —

(a) Monosubstituted derivatives of ethylenediamine showed a very close correspondence of activity *in vitro* and *in vivo*. For example considerable activity was shown both *in vitro* and *in vivo* where  $R = C_6H_5$ , i.e. N-*p*-cyclopentylbenzylethylenediamine and where  $R = C_6H_5$ , i.e. N-*p*-*n*-propylbenzylethylenediamine and N-*p*-isopropylbenzylethylenediamine. The latter compound was the only one tested also against *Leishmania tropica* *L. donovani* and *T. cruzi* and a degree of activity *in vitro* was demonstrated against these organisms similar to that displayed against *Strigomonas oncopelti*. Methylation of the benzene ring in the last-named compound apparently resulted in no great loss of activity *in vitro* or *in vivo* but introduction of an amino group on the ring led to considerable loss of activity under both these experimental conditions. Other compounds inactive *in vitro* and *in vivo* were the unsubstituted member ( $R = H$ ) and that in which an amino group occupied the position of R.

(b) There was also close correspondence between results *in vitro* and *in vivo* with several compounds of types similar to those above but containing a naphthalene instead of a benzene ring. Thus N-(1-naphthylmethyl)-ethylenediamine was only feebly active *in vitro* and *in vivo* but substantial activity was shown under both these conditions by N-(5,6,7,8-tetrahydro-2-naphthylmethyl)-ethylenediamine and N-(4-isopropyl-1-naphthylmethyl)-ethylenediamine as well as by the only non-aromatic diamine examined, N-citronallyl ethylenediamine.

(c) Among the remaining compounds tested there was less correspondence between results *in vitro* and *in vivo*. Thus a certain degree of activity *in vitro* but none *in vivo* was exhibited by the two symmetrical disubstituted compounds tested (see general formula II above) where  $R = H$  or  $C_3H_7$  (isopropyl). This was also the case with two compounds in which the ethylenediamine chain was replaced respectively by 1,6-diaminohexane and by piperazine.

(d) The reverse effect i.e. inactivity *in vitro* associated with substantial activity *in vivo* was exhibited by a phenylarsonic acid substituent of ethylenediamine  $m-O\cdot AsOH\cdot O\cdot As\ C_6H_5\cdot NH\cdot (CH_2)_2\cdot NH_2$ . This finding is in line with the well-known property of phenylarsonic acids in general, whereby activity comes into play only after reduction by the tissues to the arsenoxide form.

E. M. Lewis

LAUNOY L. Distinction, par l'action des diamidines, entre la chimio-résistance naturelle présentée par *T. congolense* et la chimio-résistance acquise par *T. annamense*. [A Distinction, shown by the Action of Diamidines, between the Natural Drug Resistance of *T. congolense* and an Acquired Drug Resistance of *T. annamense*.] *Bull. Soc. Path. Exot.* 1945 v 38 Nos. 1/2 37-42.

The author compared the action of three aromatic diamidines—4,4-diamidino stilbene (stilbamidine M. & B 744) 4,4'-diamidino diphenoxypropane [propamidine M. & B 782] and 4,4'-diamidino diphenoxypentane [pentamidine M. & B 800]—on two species of trypanosomes *T. congolense*

and a strain of *T. annamense* the latter having an acquired resistance to some compounds of antimony. The drugs were tested on these infections in mice and guineapigs.

*T. congolense*—In mice doses of 0.4 to 0.6 mgm. per 20 gm. body weight given intravenously caused a temporary disappearance of the trypanosomes from the peripheral blood but did not cure in guineapigs doses of 1 to 1.25 mgm. per 100 gm. body weight given intraperitoneally had little or no effect on the infection.

*T. annamense*—In mice 0.01 mgm. of stilbamidine caused a temporary disappearance of trypanosomes from the peripheral blood and 0.6 mgm. cured. 0.25 mgm. of propamidine cured some of the mice while 0.1 mgm. of pentamidine cured some and 0.2 mgm. cured all. In guineapigs doses of 1 to 1.25 mgm. of stilbamidine or pentamidine per 100 gm. body weight caused temporary disappearance of the trypanosomes but these doses of propamidine had no effect.

The author concludes that *T. congolense* a species with much natural resistance to drugs and this strain of *T. annamense* with an acquired resistance to some organic antimonials behaved differently towards the diamidines especially in the guineapig. [See also this *Bulletin* 1939 v 36 212.]

J. F. Corson

GOODWIN L. G. & MARSHALL P. B. The Pharmacological Properties of some Monoamidines. *J. Pharm. & Exper. Therap.* 1945 May v 84 No 1 16-25 5 figs. [11 refs.]

Data are reported on the toxicity and the effects on smooth muscle blood pressure respiration and c.n.s. of 38 compounds related to benzamidine. Most of the compounds showed depressor and spasmolytic activity. Several pyridyl monoamidines stimulated respiration and had considerable analeptic activity. Therapeutic tests in mouse trypanosomiasis (*T. equiperdum* *T. cruzi*) canary malaria and hamster leishmaniasis gave negative results.

F. C. MacIntosh

CHEN G. & GEILING E. M. K. The Determination of Antitrypanosome Effect of Antimonials in Vitro. *J. Infect. Dis.* 1945 Sept-Oct v 77 No 2 139-43 4 figs.

A method has been developed for the assay of trypanocidal substances *in vitro* based on the fact that they interfere with the metabolism of glucose by the parasites for which this substance is essential. The experiments were carried out with *T. equiperdum* which was maintained by passage in rats. The trypanosomes were isolated from the blood elements by centrifuging under standard conditions (the speed of centrifuging is given as 12 r.p.m. no doubt in error) and suspended in a medium consisting of equal volumes of rat plasma M/15 phosphate buffer pH 7.4 and Ringer Locke solution containing 0.75 per cent. glucose. Drugs were dissolved in the phosphate buffer before admixture with the other components. Over a period of 1 hour at 37°C. the rate of metabolism of glucose by the trypanosomes was constant as estimated by the ceric sulphate microtitration method (MILLER & VAN SLYKE *J. Biol. Chem.* 1938 v 114 582). The rate and degree of inhibition of glucose metabolism by drugs at different concentrations over the same period was also estimated. The percentage inhibition was used to compare the trypanocidal potencies of different antimonials and comparisons were based on the concentration that would give rise to a 50 per cent inhibition. The present results obtained *in vitro* with trivalent antimonials were in good agreement with those previously

of the important centres of oriental sore kala azar has not yet been identified. kala azar in dogs has been discovered in a number of localities since the first case was seen in Jerusalem just before the recent war. During the five years of the war 13 or more foci of canine infection have been found. It is interesting that up to the present no cases of pure cutaneous leishmaniasis in dogs have been noted, though animals suffering from kala azar may develop cutaneous lesions. It is evident that further observations are required before the complete distribution of the various types of leishmaniasis in Palestine can be estimated. The centres at present known to be infected are marked on a map of the country which illustrates the paper

C M Wenson.

SENEKJIE, H. A. & LEWIS, Ruth A. *In vitro* Effects of Specific Immune Blood on certain Blood and Tissue Flagellates. *Proc Soc Exper Biol & Med* 1945 June v 59 No. 2, 165-8.

The experiments described in this paper show that when immune sera are added to media in which certain flagellates are growing there is a specific action on the homologous organisms. Immune sera were prepared in rabbits by intravenous injection of cultures of three species of *Leishmania* (*L. donovani*, *L. brasiliensis*, *L. tropica*) and *Trypanosoma cruzi*. When these organisms were grown in rabbit blood agar containing 5 per cent. of immune sera it was found that the effect was very marked in the case of *T. cruzi* and *L. donovani* but much less so in the case of *L. tropica* and *L. brasiliensis*. In each case however, the action was on the homologous organism. The factors responsible were contained in the sera, for if washed red blood corpuscles were added to the medium instead of serum, there was no action. The factors are thermostable at a temperature of 56°C but they are partially destroyed at 70°C. Under the action of a homologous serum the culture flagellates first lose their motility and become agglutinated, later they round up and swell, while finally with lysis of the internal structures they die. It was shown that complement is not necessary for this action, and that the active principle is different from ablastin

C M Wenson

DOSTROVSKY, A. The Incubation Period in Experimental Cutaneous Leishmaniasis. *Acta Med Orientalia (Palestine & Near East Med J)* 1945 Sept. v 4 No 9 303-5

The author inoculated culture forms of *Leishmania tropica* into the skin of the left upper arms of four volunteers: the doses being 16, 4, 5 and 2 million flagellates respectively. In each case there was an immediate reaction, which, in 24 hours showed as a red area with elevated centre. Without regression these lesions developed in the next few days into typical leishmania ulcers. It is held that the large doses of flagellates injected were responsible for the clinical absence of any incubation period. *Leishmania* were found in smears from three of the ulcers. The fourth was still under observation.

C M Wenson

## FEVERS OF THE TYPHUS GROUP

HAMILTON, H. L. Specificity of the Toxin Factors associated with the Epidemic and the Murine Strains of Typhus Rickettsiae. *Amer J Trop Med* 1945 Sept. v 25 No. 5 391-5

As has already been found by other workers the complement fixation titres of sera from patients suffering from epidemic typhus were observed to be far

higher against epidemic than murine antigens so also the author found that the same sera neutralized much greater amounts of epidemic than of murine rickettsial toxins. When sera from patients suffering from endemic murine typhus were subjected to similar comparative tests it was found that the complement fixation titres indicated a high degree of specificity being much higher when murine antigen was used, but with the toxin-neutralizing tests the differences in titre were considerably less in some cases the sera were capable of neutralizing only twice to four times more murine than epidemic toxin.

This incomplete degree of correlation suggested that the complement fixing antibodies might not be the same as the toxin neutralizing antibodies. The author concludes however that the toxins associated with epidemic rickettsiae are immunologically distinct from those associated with murine rickettsiae.

John W. D. Megaw

CHUNG H. L. On the Susceptibility of *Phthirus pubis* to Infection with Typhus Virus. *Chinese Med J* Washington 1944 Oct-Dec v 62, No 4 331-3

Three batches of crab-lice were fed for seven to nine days on three typhus patients. Suspensions of the lice were inoculated into guinea-pigs which showed typical febrile reactions and not infrequently also scrotal swelling. Rickettsiae described as *R. prowazeki* were isolated from the guinea-pigs. The author suggests that in certain circumstances the crab-lice may act as a transmitter of typhus fever but he points out that the experiments do not prove that the organisms multiply in the lice which may have served merely as reservoirs of the infected blood.

John W. D. Megaw

BRUG S. L. Op Rickettsia gelijkende vormsels in de menscheijke long [Rickettsia-like Bodies in the Human Lung] Reprinted from *Nederl Tijdschr v Geneesk* 1941 Dec. 20 v 85 no 51 4636-9 9 figs (8 coloured) on 1 pl. English summary

Description of intracellular granules found in sections as well as in smears of human lungs. The granules greatly resemble Rickettsia. In 21 lungs collected at random they could be found in every case either in the smears or in the sections or in both. Probably they are normal elements of the lungs. When one is searching for virus in human material they may be mistaken for Rickettsia.

IONESCO-MIHAIESTI C. & CIUCA, M. Contribution à l'étude histopathologique de la pneumonie expérimentale chez la souris par instillation nasale de Rickettsia Prowazeki. [A Contribution to the Study of the Histopathology of Experimental Pneumonia of Mice Infected by the Nasal Route with Rickettsia prowazeki] Reprinted from *Arch Roumaines Path Expér et Microbiol* Bucharest. 1943 Jan.-Dec. v 13 Nos. 1/2 1-43 52 text figs. & 17 coloured figs. on 9 pls (15 refs.)

This monograph is profusely illustrated by 52 photomicrographs and 17 excellent coloured drawings. Full details are given of the technique employed including the use of a panchromatic stain whose composition is methylene blue 1.0 gm. toluidine blue 0.25 gm. thionine 0.25 gm. azure I 1.0 gm. McNeal's methylene violet 0.5 gm. and scarlet eosin 0.75 gm. dissolved in a mixture consisting of methyl alcohol 300 cc. glycerol 200 cc. and acetone 60 cc. Fifteen drops of the stain are added to 10 cc. distilled water. Sections are stained for one or two hours washed in distilled water dehydrated in absolute alcohol for one or two seconds then treated with a mixture of one part

oil of cloves in nine parts absolute alcohol till the sections assume a violet tint. After passing through three baths of xylol the sections are mounted in Canada balsam.

The immediate effects produced on mice by the intranasal instillation of three or four drops of suspension of heavily infected mouse lung are severe sometimes fatal, shock. When the animal recovers from this there is very soon an intense mobilization of polymorphonuclear leucocytes in the capillaries and walls of the alveoli the rickettsiae are subjected to active phagocytosis by these leucocytes in whose cytoplasm they multiply rapidly causing disintegration of the cells. Within 10 hours or so large mononuclear wandering cells begin to replace the polymorphonuclears and in turn become destroyed by the multiplication of the rickettsiae. After about 40-48 hours the fixed endothelial cells of the arteries become invaded by rickettsiae which multiply enormously in the cytoplasm often pushing the nuclei to one side and finally either rupturing the cell wall or replacing the cell by a dense mass of the organisms. These cells correspond to those described by MOOSZ as occurring in the peritoneum of rats and the tunica vaginalis of guinea-pigs inoculated by the intraperitoneal route with living rickettsiae.

The cell contents on being discharged into the alveoli and bronchioles fill these with a sero-sanguineous fluid rich in rickettsiae.

The epithelial cells of the air passages were never invaded by rickettsiae even when large numbers of these were brought into close contact with the cells.

John W D Megeay

BAUDET J & GIBAUD P. Étude histologique des lésions pulmonaires provoquées chez le lapin par l'inoculation intratrachéale expérimentale de virus du typhus épidémique. [Histological Study of Pulmonary Lesions in Rabbits due to Intratracheal Inoculation of Epidemic Typhus Rickettsiae.] *Bull. Soc. Path. Exot.* 1944 v 37 Nos 11/12, 344-7 4 figs on 2 pls.

AUBIN H. Notes sur les psychoses du typhus exanthématique. [Notes on the Psychoses of Exanthematic Typhus.] *Méd. Trop. Marseille.* 1945 Jan.-Feb.-Mar v 5 No 1 54-64

The author gives numerous examples of the various psychoses encountered in typhus fever during the incubation stage the period of defervescence and early and late convalescence. Cases are described as occurring during inapparent " " in which the real nature of the illness would have been overlooked if suspicion had not been aroused in such cases a diagnosis may be impossible unless laboratory tests are carried out.

The psychoses are not as is often stated, necessarily of the confusional type. There is sometimes evidence to show an inherited predisposition to psychosis but often the attack of typhus fever appears to be the sole cause, and when this is so the prognosis is naturally more hopeful.

John W D Megeay

GIBAUD P & GIBAUD M L. Agglutination des rickettsies test de séro-protection et réaction d'hypersensibilité cutanée. [Rickettsia-Agglutination Test Serum-Protection Test and Reaction of Cutaneous Hypersensitivity.] *Bull. Soc. Path. Exot.* 1944 v 37 Nos 3/4 84-88 1 fig

Large numbers of the tests were carried out, many of them comparative. The rickettsia agglutination test employed was a modification of the original Weigl test. Rickettsia suspensions were made from infected mouse lungs which were ground up in formalized saline and freed from large particles by decantation. Seven droplets of the suspension were placed separately on a slide and to each was added a droplet of one of seven dilutions of the serum

to be tested ranging from 1-10 to 1-640. The slide was at once placed in a Petri dish containing a little water to prevent evaporation. After 12 hours at room temperature the slide was taken out and the droplets were allowed to dry. The films were fixed in methyl alcohol washed in water and stained for half an hour with a mixture of five drops of Giemsa stain and 1.0 cc. boiling neutral distilled water. After differentiation in equal parts of absolute alcohol and xylol the film was washed and dried. The degree of agglutination is said to be sharply defined ranging from coarse dense clumps to very small clumps among scattered free organisms.

The tests of human sera were carried out immediately before each of three injections of rabbit lung vaccine given at weekly intervals and a week after the last injection. The highest titre was usually reached a week after the second dose of vaccine but the responses were very varied the titres ranging from 1-10 to 1-640 and averaging 1-80 to 1-160. The sera of patients suffering from severe attacks of typhus fever reacted at high titres such as 1-1 500 in mild, pseudo-influenza attacks the titres usually were 1-80 to 1-160. The reaction soon became negative.

The serum protection tests were carried out by mixing the serum with varying dilutions of virulent rickettsial cultures keeping the mixtures for half an hour at 37°C and injecting them intradermally into a rabbit. As a control the same culture without serum was injected into another part of the skin of the same rabbit.

The sera of vaccinated persons showed protective reactions of progressively increasing strength after successive doses of the vaccine. After mild attacks of typhus corresponding reactions occurred after severe attacks still stronger reactions were observed, and they remained positive for many years.

The intradermal hypersensitivity test is based on the local inflammatory reaction produced in typhus patients by intradermal injections of killed rickettsia cultures. This reaction gave very varying results it usually remained negative after protective vaccination with killed rickettsiae but after vaccination with living rickettsiae and after mild attacks of typhus it soon became positive. After severe attacks the reaction was slow in appearing sometimes it was delayed for months. It remained positive for years after the attack.

There was no agreement between the responses to the serum-protection and rickettsia-agglutination tests the latter gave irregular and inconsistent results but the serum protection test gave results consistent with the amount of antigen injected. The rickettsia agglutination test was regarded as indicating the presence of antibodies of infection rather than of immune anti bodies.

SUREAU B Elimination d'agglutinines antirickettsiales par les urines albumineuses du lapin inoculé par voies dermique ou péritonéale [Discharge of Anti-Rickettsial Agglutinins through the Albuminous Urine in Rabbits Inoculated Subcutaneously and Intraperitoneally] *Bull. Soc. Path. Exot.* 1945 v 38 Nos 7/8 185-7 1 fig

Rabbits were inoculated with living typhus rickettsiae when the agglutination titre of the serum had reached a height of about 1-160 an artificial nephritis was produced by a bismuth preparation injected daily for a week. When the albuminuria became pronounced agglutinins appeared in the rabbits urine reaching a titre of rather less than 1-40 and simultaneously the agglutination titre of the serum fell to less than 1-80. With the disappearance of the albuminuria the agglutinins also disappeared from the urine and the agglutination titre of the serum rose slightly remaining constant for some time at about 1-80.

John W D Megaw



GIROUD P & SUREAU B. Les variations des agglutinines de la peau inoculée et saine chez le lapin infecté par virus typhique avec du virus typhique. [Variations in Agglutinins from Inoculated and Healthy Skin in Rabbits Infected Intradermally with Typhus Rickettsias] *Bull. Soc. Path. Exot.* 1944 v 37 No 9/10 264-8 1 fig

V BORMANN & PREUSS Zur Schnelldiagnose des Fleckfiebers aus dem Blutstropfen. The Rapid Diagnosis of Typhus Fever by Blood Droplets Slide Test. *Ztschr. f. Immunopath. u. Exper. Therap.* 1944 Nov 18 v 105 No 4 313-30 1 fig [11 refs.]

The most useful feature of this paper is that it contains a summary of the numerous rapid modifications of the Weil-Felix and other agglutination tests. The authors give details of the method adopted by themselves in carrying out one of these modified tests in which dried cultures of *Proteus O 19* prepared by a proprietary firm, are used for the suspensions. They lay special stress on the employment of drops of suspension not larger than the drops of blood under test.

Their claim that the test is more reliable than the standard test does not appear to be valid. Among 46 patients suffering from diseases other than typhus fever and tested by their method, there were 19 positive reactions as compared with four with the standard test. Although they claim that in 378 samples of blood from typhus patients there were 103 negative responses as compared with 121 with the standard test the basis of comparison seems to be unfair because no account is taken of standard reactions at titres below 1-400 all these are included among the negative responses and their number is not stated.

John W D McGraw

ORTIZ MARIOTTE C. MALO-JUVERA F & PAYNE G C Control of Typhus Fever in Mexican Villages and Rural Populations through the Use of DDT *Amer. J. Pub. Health.* 1945 Nov v 35 No. 11 1191-5 1 fig

In two Mexican villages epidemics of typhus fever were promptly controlled by dusting the clothing of the great majority of the inhabitants with a powder containing 5 per cent DDT. In one village 612 of the 671 inhabitants were treated, and in another 739 out of 1016. Each person's head was treated with a lotion whose active principle was phenyl cellosolve [see this *Bulletin* 1944 v 41 744]. In both villages the disinfection was started while the epidemic was approaching its peak and allowing for the incubation period, the abrupt cessation was what would have been expected, assuming complete efficiency of the method.

Experiments were carried out in typhus-free villages in one with a house infestation rate of 33 per cent the clothing was treated twice with a seven-day interval two weeks later the infestation rate was 1.6 per cent. six weeks later it was 1.1 per cent. three months later it had risen to 9.5 per cent. In another village a single treatment reduced the rate from 60 to 11 per cent. two months later it had risen to 26 per cent.

The effect of phenyl cellosolve on head lice was

NEUJEAN G Études sur les Rickettsioses. Problèmes posés. Critique des méthodes diagnostiques et de recherche. [Studies of Preliminary Note II. Presented and New Methods for use in Congo Belge. 1945]

Some of the findings are so revolutionary that they require confirmation.

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likely to 1

In Part I the author refers to his previous description of an epidemic in Ruanda Urundi in 1939-40. In this the rickettsiae were regarded as being murine though they seldom caused an orchitic reaction and were abnormal in some other respects. The organisms were isolated from lice, bed bugs, fleas and ticks in some of the outbreaks. The vector chiefly incriminated was the bed bug. The mammalian reservoir was the rat in which a very high percentage rate of infection was found in the affected areas. The Weil-Felix reaction was of the *Proteus* OX19 type but in recent outbreaks the OXA type has become increasingly frequent. Few fatalities occurred but in some severe attacks an inoculation eschar like that of boutonneuse fever was seen.

In Part II the opinion is expressed that rickettsiae are closely related to protozoa. The fallacies connected with the usual methods of diagnosis and research are discussed, including the anomalous results often obtained by animal experiments and the Weil-Felix test. Strict adherence to the technique of FELIX and BRIDGES [this *Bulletin* 1944 v 41 552 & 554] is recommended. Great advantages are claimed for the staining method of LESTOQUARD, briefly this consists in fixing for 5-10 minutes in a mixture of 98 parts of 94 per cent alcohol and two parts of fresh tincture of iodine, washing in alcohol, drying, staining for one or two hours in a mixture of 1.0 cc. distilled water (pH 7.4) and three drops each of May-Grunwald and Giemsa stain, differentiation by alcohol and washing in neutral distilled water. Using this method the author claims to have shown the frequent presence of rickettsiae in the urinary sediment obtained by centrifugation in the sputum, the conjunctival secretion, the nasal mucus and in skin scrapings obtained by the method used in the search for leprosy bacilli.

He states that rickettsiae can easily be cultivated by adding the patient's blood to normal saline, great multiplication of the organisms is said to occur in the infected white cells within a period ranging from a few hours to two or three days.

The most surprising claim of all is that during the prevalence of the disease of Léopoldville rickettsiae were found in the blood of all the 50 persons examined whether they were sick or healthy. This universal occurrence of the organisms is regarded as being comparable with what happens in malaria (presumably in areas of hyperendemicity).

Examination of the urine gave positive results only when the disease process was active. Pronounced rickettsial infection was found in the liver cells of patients who had been retrospectively diagnosed as suffering from yellow fever because of the histological changes found in the organ. *John W. D. Megaw*

PANG K. H. *Studies on Typhus Fever Epidemic occurring in a Poor House II. Etiological and Epidemiological Studies.* *Chinese Med J* Washington 1944 Oct.-Dec. v 62 No 4 334-46 [23 refs]

This epidemic occurred in a poor house where 570 persons were living in deplorable conditions in rooms infested with rats. The conditions appear to have been eminently suitable for the occurrence of both louse-borne and flea-borne typhus.

Among 248 children under 11 years there were 11 cases in the 11-15 age group there were 23 cases among 196 children and among the remaining 130 persons there were 4 cases. Two girls living in one room were attacked on April 5 1940, another girl in the same room was attacked on May 26 and then cases began to occur in various rooms. After August 22 there were no further cases till April 25 1941 when three girls occupying a rebuilt and relatively rat-free room were attacked and during the next two months six further cases occurred.

Numerous strains of rickettsiae were isolated by guinea-pig inoculation of these seven were from patients eight from rats and their fleas four from body lice of patients ten from body lice of healthy inmates and one from a rat mite.

Obvious orchitis appears to have occurred in only one of the many guinea-pigs used for inoculation or transfer of the strains but rickettsiae were often detected in vaginal smears. The infection is stated to have died out after a few passages in guinea-pigs.

During the period of the main epidemic only four of the 18 rats examined were infected and in the inter-epidemic period seven of 12 rats were found infected.

Inoculation experiments with batches of lice collected from healthy inmates gave the following results—one batch collected May 18 1940 was infected two batches collected June 17 and 25 1940 at the height of the epidemic, were infected only one among ten batches collected during the winter epidemic period up to January 1941 was infected between February and April 1941 "most of the batches examined were infected," and during the recrudescence of the infection all the three batches tested were infected.

All the strains isolated were regarded as murine but transmission was believed to be by lice

John W D Meager

PANG K. H. ZIA, S. H., CHEN S. M. & FENG Y. S. Studies on Typhus Fever Epidemic occurring in a Poor House. III. Control Measures, with special reference to the Use of Typhus Vaccine. *Chinese Med. J.* Washington. 1944 Oct.-Dec. v 62, No. 4 347-50.

The author describes the results obtained by the use of a locally prepared tissue-culture vaccine in the control of an institutional epidemic.

Among 97 vaccinated girls there were five attacks (5.2 per cent.) against nine attacks (9.6 per cent.) among 106 non-vaccinated girls living in closely similar conditions. No mention is made of any difference in the severity of the attacks in the two groups the disease is stated to have been mild, and there were no deaths. Part I of this series has not been traced, the reference to it as given by the authors is incorrect.—Ed

John W D Meager

RUGIERO H. R. & COHEN J. Nuevos casos de tífus exantemático en la Ciudad de Buenos Aires y sus alrededores. [Further Cases of Exanthematic Typhus in Buenos Aires and its Environs.] *Revista Méd. Argentina.* 1945 Nov 9 v 32, No. 45 2203-6.

The authors have seen 11 cases of murine typhus fever in and near Buenos Aires between August 1944 and July 1945.

The cases were sporadic but six of the patients, who were attacked in January and February 1945 had been working on the same floor of a rat-infested grain store

John W D Meager

ANDERSON W. L. & WING W. M. Tsutsugamushi Disease (Scrub Typhus) a Clinical Study of Forty Nine Cases. *War Medicine* Chicago. 1945 Sept. v 8 No. 3, 163-6

Brief clinical notes are given of 49 cases of tsutsugamushi fever which occurred in a Pacific Island among 750 soldiers who had bivouacked on a grassy plain previously occupied by Japanese troops.

The percentage incidence of the chief features was—headache 98 backache 90 chills 30 deafness 15 respiratory-system involvement 10 adenopathy

90 eschar 70 rash 43 palpable spleen 40 tender lymph nodes 35  
bradycardia 100 *Proteus* OXA agglutination reaction 53 leucopenia 40  
minor abnormality of urine 30  
In many cases there were multiple eschars. A reference is made to the  
occurrence of infected bites of men from the same patrol hospitalized for other  
causes. These lesions are said to have had a different distribution on the body  
but they are not described.  
The island had been reported to be free from infection and the authors  
remark that if that is true it must be assumed that the disease had been  
introduced by the Japs but he rightly suggests as a much more likely explana-  
tion that the disease had existed without being recognized.

John W D Megaw

HOWELL W L. Absence of Electrocardiographic Changes in Tsutsugamushi  
Fever (Scrub Typhus). Report of Two Hundred Consecutive Cases. *Arch  
Intern Med* 1945 Oct. v 76 No 4 217-18.

- 1 An electrocardiographic study was made of 200 consecutive patients  
convalescent from tsutsugamushi (scrub typhus) fever
2. No abnormal electrocardiographic patterns were found.
- 3 The incidence of isolated deviations from the normal was no higher than  
that found in the electrocardiograms of healthy persons of the same age

BLAKE F G MAXCY K F SADUSK J F Jr KOHL G M & BELL, E. J  
Tsutsugamushi Disease (Scrub Typhus, Mite-borne Typhus) in New Guinea.  
*Amer J Pub Health* 1945 Nov v 35 No 11 1121-30 1 map [25 refs]

This is a review article most of the information has already been abstracted  
see this *Bulletin* 1945 v 42 991 993

SOMERS R B U A Case of Tick Typhus in the Sudan. [Memoranda.] *Brit  
Med J* 1945 Dec 15 648 1 chart.

The special interest attaching to this case is that it is the first to be reported  
from the Anglo-Egyptian Sudan. The patient was an English schoolmaster  
engaged in inspecting bush schools.

The fever was predominantly of a deep remittent type. It lasted about  
10 days. The pulse rate was slow never exceeding 76 on one occasion when  
the temperature was 103°F it was 64.  
A *tache noire* was present this had been seen by the patient about 10 days  
before the onset. No tick had been detected. There was a maculo-papular rash  
with a tendency to vesication in some of the spots. The rash was abundant on  
the forearms and scanty on the trunk. *Proteus* OX2 was agglutinated at a  
titre of 1-500; with OX19 the reaction was negative.

John W D Megaw

LE GAC P & BORJEL, L. Premier cas de fièvre boutonneuse au Togo. [The  
First Case of Boutonneuse Fever in Togo] *Bull Soc Path Exot* 1945 v  
38 No. 9/10 247-50

BOW M R & BROWN J H. Tick-borne Diseases of Man in Alberta  
[Canadian Med Ass J] 1945 Nov v 53 No 5 459-65 1 map [48  
refs]

The authors give short notes on the history, epidemiology and clinical  
aspects of Rocky Mountain spotted fever tick paralysis and tularemia with

[April, 1946]

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special reference to their occurrence since 1833 in the Province of Alberta Canada. Six known cases and one suspected case of Rocky Mountain spotted fever have been reported in Alberta there have been two cases of tick paralysis and two cases of tick transmitted tularemia in man. In the authors opinion the tick borne diseases of man are important in Alberta they appear at present to be confined to the southern part of the Province but there are indications that further survey work might disclose a similar situation in the foothills and mountain area.

The following ticks capable of transmitting tularemia have been collected in Alberta — *Dermacentor andersoni* *Harmaphysalis leporispalustris* (rabbit tick) and *Harmaphysalis rickettsi* (bird tick) *D. andersoni* infected with *Demacentromerus rickettsi* (*Rickettsia rickettsi*) and with *Pasteurella tularensis* has been collected in the southern area of the Province.

[PARKER et al. (Public Health Reports Washington 1932, v 47 479) found strong presumptive evidence that *H. cinnabarina* transmitted tularemia in sage hens but no proof that it had been implicated in human disease.]

J F Corson.

PARRON G. La fièvre des tranchées existe-t-elle en Algérie? (Does Trench Fever occur in Algeria?) Arch. Inst. Pasteur d'Algérie 1945 Sept. v 23 No. 3 180-82 1 chart

The author describes a case of fever which conformed in all its clinical features to one of the types of trench fever. There were three spells of fever each lasting about three days the spells started on the 1st, 7th and 14th days. The fever curve was of the undulant type and the total duration was 14 days. Severe nocturnal pains of the shin-bone type occurred and convalescence was slow. Repeated blood examinations including culture tests gave negative results and the author was satisfied that relapsing fever undulant fever malaria and typhoid-group fevers could be excluded. He suggests that some of the numerous cases diagnosed in Algeria as relapsing fever without spirochaetes may be examples of trench fever.

John W D Megey

## YELLOW FEVER

BATES M & ROCA-GARCIA M. The Douroucouli (Aedes) in Laboratory Cycles of Yellow Fever Amer J Trop Med 1945 Sept. v 25 No. 5 383-9 2 figs.

Four douroucouli (*Aedes triseriatus*) from the Villavieja area of eastern Colombia were tested in laboratory cycles of yellow fever with the mosquito *Harmagogen capricornis* and a local strain of virus. All four animals showed acute fatal infections characterized by fever and a very high titer of circulating virus death occurred on the fourth or fifth day after infection. Three of the animals showed stomach hemorrhage and liver tissue from all four showed lesions characteristic of fatal yellow fever in man and rhesus monkeys. Virus was transmitted by the bite of the mosquito *Harmagogen capricornis* from squirrel to douroucouli douroucouli to douroucouli and douroucouli to samuri. There is some evidence that the douroucouli may be important in the epidemiology of yellow fever since it is said to be the only monkey in certain areas in Colombia where the disease is endemic.

ERRERO A. *L. Aedes aegypti*. Le danger qu'il représente pour l'agglomération Algéroise [*Aedes aegypti* Its Danger to Algeria.] [Thésis.] 100 pp 1 folding map & 4 figs. [Bibliography.] 1939 Algiers La Typo-Litho et Jules Carbonel réunies.

FAVAREL R. Immunisation du cobaye contre le virus de la fièvre jaune par scarifications cutanées [The Immunization of the Guinea pig against Yellow Fever Virus by Cutaneous Scarification.] *Bull Soc Path Exot* 1945 v 38 Nos 3/4 77-86

The author inoculated 11 guinea pigs with neurotropic yellow fever virus the French strain at its 216th passage in mice and 6 guinea pigs with culture virus 17D reinforced by 10 mouse brain passages and growth again on chick embryo. In both series the cutaneous scarification method was used.

Out of the 11 animals vaccinated in this manner with the neurotropic virus 7 were completely resistant to an intracerebral inoculation of several thousand lethal doses 35 to 47 days after being immunized. On the contrary all 6 guinea pigs vaccinated in the same way with the culture virus succumbed to yellow fever encephalitis when inoculated intracerebrally with virus 25 to 50 days after the scarification. Out of 5 guinea pigs scarified with neurotropic virus which all gave negative mouse protection tests two were resistant when inoculated intracerebrally with the virus showing that an animal may be immune without the blood containing immune bodies in sufficient quantity to give a positive test.

The divergent results obtained with these two strains may be explained as due to the difference in neurotropism. One could also suppose that one strain had a greater affinity for the skin of the guinea pig.

In the discussion Dr STEFANOPOULO in whose laboratory the work was performed emphasized that in the case of bacterial infections it is necessary to use a larger dose of an attenuated strain than of a virulent strain in order to produce infection. Normally the guinea pig is not very susceptible to yellow fever virus and with culture virus it is probably necessary to use larger doses to produce immunity. He also mentioned that vaccination of human beings with culture virus by the scarification method is often insufficient to ensure protection but that subcutaneous inoculation of the same virus is efficacious.

E Hindle

### DENGUE AND SANDFLY FEVER.

FAIRCHILD L. M. Dengue-like Fever on the Isthmus of Panama. *Amer J Trop Med* 1945 Sept. v 25 No 5 397-401 3 figs

The author studied 32 cases of a short fever seen in the Panama-Canal Zone between September 1941 and March 1942.

Among 21 cases in which the fever curve was available 13 were of the two-phase saddle back type and 7 of a continuous spiking type. The total duration of the fever in both types was about five days.

A blotchy macular rash was seen in every case. One or more groups of lymph nodes were enlarged in five cases. The leucocyte count ranged from 2 000 to 6 000 per cmm. The lymphocytes were more than 40 per cent of the total white cells in the 16 cases in which there was leucopenia.

The author discusses at some length the features in which the symptomatology differed from that described by certain authors as being characteristic of

dengue but in view of the well-known variability of that disease and of the known occurrence of outbreaks in the region there seems to be no good reason for hesitating to place the fever in the dengue group. *John W D Megaw*

CULLINAN E. R. Immunity to Sandfly Fever [Memoranda.] *Brit Med J* 1946 Jan. 5 12.

An outbreak of sandfly fever occurred in a hospital in the Middle East in the summer of 1942 [see CULLINAN & WHITTAKER, *this Bulletin* 1944 v 41 125] and in the summer of 1943 another outbreak occurred in the same hospital. In the first outbreak several persons had more than one attack, which suggested that an attack conferred no early immunity.

In the second outbreak in 1943 55 out of 142 (about 39 per cent.) of persons who were not present during the 1942 outbreak were attacked while only 13 out of 98 persons (about 13 per cent.) who were present in 1942 were attacked. The author thinks that this evidence suggests that while an attack of sandfly fever does not confer an early immunity or at most a very short-lived one it may confer a more distant immunity. [See also LEVSHITZ *this Bulletin* 1944 v 41 506.] *J F Corson*

## PLAGUE.

DEVIGMAT R. SCHÖETTER M. & GILLÉ SÉVIL Mme. S. Quelques considérations sur la peste du cobaye. [Notes on Plague in the Guinea-pig.] *Rev. Travaux Sci Méd Congo Belge* 1945 July No. 4 25-36 3 diagrams.

A periodic extraction of data from routine records is a useful and serviceable exercise especially when assisted by personal memory. In the campaign against plague on Lake Albert in the Belgian Congo the laboratory at Bukwa has played a notable part. Since 1898 more than 12 000 guinea-pigs have been inoculated in various ways with plague material, and more than 800 of these dead of plague, have been subjected to autopsy. The different modes of inoculation are classified as: subcutaneous, conjunctival, on scarified skin and other ways. The discussion in the text accompanied by graphs and detailed tables relates to:—A. Standard infecting dose. B. Inoculation by different methods and C. Data of preventive vaccination and serum prevention. This discussion is summarized:—(1) Autopsies showed three different types: (a) the violent septicaemia with hypertrophy of liver and spleen; (b) the moderate form in which liver and spleen are enlarged and mottled; and (c) that of partial resistance, where liver and spleen seem pseudotuberculous while the lung is consolidated (hepatization) and covered with whitish tubercles. (2) The duration of life is shown as a graph of the number of guinea-pigs dead on each successive day after a virulent inoculation. With a strain of maximal virulence "say the authors and inoculation of 10 lethal doses (54 to 155 organisms) we obtain a curve which we put forward as a unit of virulence for the determination of the severity of routine inoculations and ultimately of protection by vaccine or serum. The authors consider that this graphic method is more expressive than the simple presentation of the crude figure giving the percentage of animals dead and surviving." *W F Harvey*

COLE L. C. The Effect of Temperature on the Sex Ratio of *Xenopsylla cheopis* recovered from Live Rats *Pub Health Rep Wash* 1945 Nov 9 v 60 No 45 1337-42. [14 refs]

The danger of plague in an area is often considered to be proportional to the flea population particularly of *Xenopsylla cheopis*. The flea population is usually estimated by flea counts from trapped rats but these counts do not always give an accurate estimate of the total natural population. This paper attempts to relate the results of flea counts to the total flea population and to show how temperature changes in the environment may affect the results. Male and female fleas apparently exist in approximately equal numbers but whereas at low temperatures (below 70 F) females usually predominate in captures from rats at high temperatures (over 75°F) males are caught in greater numbers. This rise in the proportion of males captured at higher temperatures is due to an increase in the number of males found on the rats rather than to a fall in the number of females. It is suggested that the flea index should perhaps be computed for female fleas only.

Kenneth Mellanby

KALMBACH E. R. "Ten-Eighty", a War-Produced Rodenticide *Science* 1945 Aug 31 232-3

The substance referred to is sodium fluoroacetate. Its toxicity to small mammals was found during the course of the long-established search for new rodenticides carried out by the Wildlife Research Laboratory in Denver. Compound 1080 as it is known is extremely toxic to many small mammals and also to domestic animals such as cats and dogs and is a possible danger to man especially to operators who may use it carelessly. The following table gives the LD50 values —

	Mg/kg
Leghorn hens	10.00
Deer mice ( <i>Peromyscus</i> )	5.0
Wood rat ( <i>Neotoma</i> )	5.0
Wild Norway rats ( <i>R. norvegicus</i> )	5.0
Tame white rats	2.5
Black tailed prairie dogs ( <i>C. ludovicianus</i> )	2.5
Meadow mice ( <i>Microtus</i> )	0.5
Domestic dogs	0.35
Fisher's ground squirrel ( <i>C. beecheyi fisheri</i> )	0.35
Wild black rats ( <i>R. rattus</i> subsp.)	0.1

Compound 1080 is very soluble in water and the results in rat control of exposing a solution have seldom, if ever been matched by other control methods. Similar results have been recorded when the material has been used on grain baits against field rodents.

Charles Wilcocks

RICHTER C. P. The Development and Use of Alpha-Naphthyl Thiourea (Antu) as a Rat Poison. *J Amer Med Ass* 1945 Dec 1 v 129 No 14 927-31 [Refs in footnotes]

This paper contains the first detailed announcement of the development of a new rodent poison by a team of the Johns Hopkins University working under a contract with the Office of Scientific Research and Development. Alpha-naphthyl thiourea is a fine grey powder highly insoluble in water or acid solutions slightly more soluble in alkalis stable under normal conditions and with a melting point of 184°C. It is said to have the following LD50 though the details of toxicity tests on which such figures are based are not given.



*Rattus norvegicus* 7 mgm. per kilo *Rattus rattus* squirrels and guinea pigs 100-400 mgm. per kilo mice and dogs less than 100 mgm. per kilo Monkeys rabbits and chickens were more resistant and "5 Gm. per kilogram was required to kill 100 per cent. of groups of chickens and monkeys. In an extensive campaign in Baltimore it has been used in a mixture (2 to 5 per cent.) with finely ground grain such as maize or wheat and as a dust either on vegetable foods or blown in runways or on the surface of water. These tests have been in most areas 90 per cent. effective though no detail is given as to how such estimates were arrived at. In Norway rats and dogs death is due to drowning from pulmonary oedema a very large lymph flow through the capillaries of the lungs being produced. No antidote is known though the low solubility of the compound makes stomach lavage a useful countermeasure in cases of accidental poisoning.

R. B. Freeman.

## CHOLERA

FELSENFIELD O & YOUNG Viola M Simultaneous Vaccination against Bacillary Dysentery and Cholera with Toxoid Vaccine *Amer J Trop Med* 1945 Sept v 25 No 5 421

Experiments were made to produce a reliable combined vaccine against cholera and bacillary dysentery. *Vibrio cholerae* (Inaba Ogawa and El Tor strains) *Shigella dysenteriae* and *Sh. paradyenteriae* Y were used.

*Sh. dysenteriae*—Several methods of preparation were tried and it was found by mouse protection tests that the strongest immunity was produced by a combination of alcohol-killed organisms and formalized culture filtrate.

*Sh. paradyenteriae* Y—The same procedures were used except that culture filtrate was not tried the most effective vaccine was prepared from alcohol-treated organisms.

*V. cholerae*—The best results were obtained with formal killed or heat killed Inaba organisms combined with formalized filtrate of Inaba or El Tor strains (the El Tor strain being finally selected).

All vaccines retained their immunizing power much longer when desiccated in a vacuum.

Tests on volunteers showed that formalized organisms combined with formalized filtrate gave rise to the strongest and most lasting antibody production. A mixture of antidyentery and anticholera vaccines did not cause more severe reactions than either alone and produced a satisfactory increase of antibody formation which persisted for a considerable length of time.

The findings indicate that continuation of these experiments is fully warranted.

J F Corson

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

TSUCHIYA H. Survival Time of Trophozoites of *Endamoeba histolytica* and its Practical Significance in Diagnosis. *Amer J Trop Med* 1945 May v 25 No. 3 277-9

The author has studied *E. histolytica* as it occurs in stools kept at room temperature (22°-25°C.) incubator temperature (37°C.) and refrigerator temperature (5°C.) At room temperature the survival time of six different strains

was 6 to 16 hours. In the refrigerator it was 48 to 96 hours while in the incubator it was only 3 to 5 hours. It is evident that for diagnosis the best procedure is to examine the fresh specimen but if this must be kept before examination it may be left at room temperature for a few hours. If a longer delay is contemplated then the refrigerator is the best. In no case should the specimen be left in the incubator. Amoebae which were quite motionless after exposure to cold often resumed their activities when examined in the warm chamber. In some cases amoebae which were unidentifiable in the kept stool regained their specific characters when cultivated in suitable media. A strain of trichomonas was found to survive for 21 days at 5°C and for 15 days at 22°C. When the stool was exposed to 37°C the organism multiplied profusely for a few hours and then disappeared.

TAN C C & LI 1. *Amoebic Colitis with special reference to Perforation. A Study of 20 Autopsied Cases. Chinese Med J* Washington 1944 Oct.-Dec v 62 No 4 368-76 6 figs

Autopsy was done on twenty cases of amoebic colitis in all of which there had been clinical evidence of the condition during life. The ages of the 349 patients from whom these were obtained ranged from 3 to 62 years the majority being in their fourth decade. In half the cases coming to autopsy there was diffuse amoebic involvement of the colonic tract involvement of the sigmoid was seen in 17 of the 20 (85 per cent) of the caecum in 16 (80 per cent) and of the rectum, ascending and descending colon each in 15 (75 per cent) and of the transverse colon in 12 cases (60 per cent). The terminal ileum was involved in 7 (35 per cent) and liver abscesses were found in 6 of the 20 cases all being in the right lobe of the liver. In 11 of the 20 cases the fatal attack of amoebic dysentery was the first attack and in 6 of these clinically primary cases there was perforation of the gut. In 3 other cases of perforation there was a history of amoebic dysentery before the fatal attack. A diagnosis of perforation was made *ante mortem* in 6 of the 9 cases where its occurrence was established *post mortem* and 6 of the 9 had received emetine either just before or after the perforation occurred. The ninth patient was moribund on admission and died in a few hours. Only one of the authors diagnosed cases of amoebiasis with intestinal perforation recovered and here spontaneous discharge of a localized abscess took place through the abdominal wall. In 5 of the total 10 (including the patient who recovered) the perforation occurred in the caecum in 4 in the descending colon in 2 in the sigmoid and in one in the transverse colon. Multiple perforation was found in 2 cases. The authors regard this complication as almost invariably fatal its diagnosis is difficult and its treatment with emetine ineffective. A R D Adams

COTTRELL J D & PEDDIE J J G. *The Diagnosis and Treatment of Chronic Amoebiasis. New Zealand Med J* 1945 Oct v 44 No 243 230-41

This paper has been written to acquaint the medical practitioner with the problems of amoebiasis in the returned soldier. It gives a good account of the condition but contains nothing original other than such statements as 'no soldier with recurrent or chronic diarrhoea should ever be dismissed as incurable until he has had the benefit of at least one full course of anti-amoebic treatment—in spite of repeated negative stool examinations and speaking of emetine. In emergency one or two doses may be given intravenously and again of quinoxyl enemata. Even a 10% solution may be used in refractory cases. A R D Adams

HOWELL, G. Two Cases of Amoebic Granuloma. *Brit. Med. J.* 1946 Feb. 2, 181-2.

BRUCKMANN, G. & WERTHEIMER, E. A Study in the Toxicology of Emetine. *Acta Med. Orientalis (Palestine & Near East Med. J.)* 1945 Sept., v 4 No. 9 291-4.

It has been repeatedly said that the therapeutic effect of emetine would probably be much greater if the tolerated and toxic doses were more widely separated. It was for long known to be a "general irritant and protoplasmic poison" and more recently damage to the heart and the cornea has been described. The authors have taken in hand a more intensive study of the drug toxicologically as regards its impairment of liver function and its influence on carbohydrate metabolism, the part played by the liver in detoxification of emetine and the influence of diet on the toxicity of the drug.

Male white rats were the animals used. The description of the results is confusedly written. Thus the authors state "a single high dose of emetine was given and the animals were killed from 2 to 17 hours later" and they continue directly as follows "The higher dose 2.0 mgm. per 100 gm. rat was always fatal in 5 days" smaller doses 0.6-1.3 mgm. resulted in symptoms of emetine poisoning, but were not fatal. The higher doses caused a marked fall in liver glycogen smaller doses less. Because the body temperature fell sharply this was considered to be due not to any specific action of the drug, but to shock. To distinguish the specific influence of the drug in small doses on carbohydrate metabolism, animals were injected with doses of 0.3 mgm. and one such and one of a control group were sacrificed for glycogen determination. Under these conditions the temperature remained unchanged for 10 days but food was refused and weight began to fall after the 6th day. By feeding the controls on the same amount of food as the experimental animals had taken the previous day starvation glycogen values could be eliminated. There were no indications that repeated small doses of emetine impaired the liver function seriously.

To test the action of the liver in the detoxification of emetine the mortality among rats in which two-thirds of the liver had been removed and that among others not so treated, the animals being injected with the drug, was observed. Mortality was found to be higher among the hepatectomized rats except in those which lived for more than seven days by which time it is said, the liver tissue had been regenerated. The authors rightly point out that the fact of an organ being concerned in the detoxification of a poison does not necessarily mean that the organ is damaged by the poison.

Lastly to test the influence of diet on the toxicity of emetine the drug was given to rats on six different diets, the essential principles of which are detailed in the paper. It was found that adding protein to a balanced diet did not prolong the life of the rats although a reduction of protein lowered the animal's resistance to emetine. This reduction of resistance is ascribed to the probable impairment of hepatic function.

H. Harold Scott.

LIBBERMANN, H. R. *Isospora hominis* causing Acute Gastro-Enteritis in Man. *South African Med. J.* 1945 Sept. 22, v 19 No. 18 341-2 4 figs.

The patient described was a middle-aged European who had been living in a military camp in Durban for six months. A severe attack of gastro-enteritis with vomiting and diarrhoea developed one evening. This lasted for 72 hours. Bacteriological examination threw no light on the condition, which was not experienced by any other person in the same mess. Microscopical examination revealed *Entamoeba coli*, trichomonads, Charcot-Leyden crystals and red blood corpuscles as well as numerous oöcysts of *Isospora hominis*. The last named

persisted for more than 14 days by which time all symptoms had disappeared. After the patient had returned from two weeks sick leave they could no longer be found. It is concluded that the coccidian was the cause of the patient's illness.

C M Wenyon

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES.

LOFGREN Ruth & SOULE M H The Effect of Low Temperature on the Spirochetes of Relapsing Fever I. The Viability of Four Strains of Spirochetes stored at  $-48^{\circ}\text{C}$ . II. The Structure and Motility of *Spirochaeta novyi* J Bacteriology 1945 Sept v 50 No 3 305-11 313-21 3 figs

The four strains used in this work *Spirochaeta duttoni* *S. hooki* *S. novyi* *S. obermeieri* had been maintained in rats for some 40 years. During the course of infection spirochaetes appear in the blood 24 hours after inoculation increase rapidly up to the 4th day and then suddenly decrease.

In the experiments blood was taken from the heart defibrinated by whipping and centrifuged. The layer of spirochaetes above the red cells was mixed with the serum and distributed in 0.2 ml. amounts in Cellophane tubes. After freezing in an alcohol-carbon dioxide mixture the tubes were stored for various lengths of time at  $-48^{\circ}\text{C}$ . The organisms were then tested for infectivity by sub-inoculation into rats.

Spirochaete suspensions obtained on the 2nd day of disease remained infective for at least 27 months whereas spirochaetes taken on the 3rd day or later became non infective after a few days.

In a later experiment it was found that 3rd day spirochaetes were still infective after two years provided the original material consisted almost entirely of spirochaetes. The authors consider that this increased viability depends on the number of organisms in the original specimen.

A study was made of the morphology of normal forms of *Spirochaeta novyi* as compared with spirochaetes stored for seven days at  $-48^{\circ}\text{C}$ . and spirochaetes which had been repeatedly frozen and thawed [the detailed descriptions cannot be summarized]. Observations on the effect of variations of temperature on motility were carried out with the help of a warming and cooling stage. The temperature of a suspension of *S. novyi* was raised to  $37^{\circ}\text{C}$ . gradually lowered to freezing point and the cycle repeated until the organisms died. The degree of motility was noted at temperature differences of  $5^{\circ}\text{C}$ . It was found that motility diminished as the temperature fell was abolished at zero and was regained, but to a lessened degree as thawing occurred. After three freezings and thawings practically all the spirochaetes were dead.

J C Broom

WOLMAN B & WOLMAN M Studies of the Biological Properties of *Spirochaeta recurrentis* in the Ethiopian High Plateau. Ann Trop Med & Parasit 1945 Oct. 10 v 39 No 2 82-93 [27 refs.]

A description of studies on the properties of an Abyssinian strain of the spirochaete of louse-borne relapsing fever carried out at Addis Ababa, Ethiopia.

The spirochaetes were cultivated in a medium composed as follows. One cc. of egg albumin was coagulated in a sloping test tube by heating to  $80^{\circ}\text{C}$ . To this was added about 10 cc. of a mixture of sterile human ascitic fluid 1 part, buffer solution (of pH 7.8) 2 parts and saline 2 parts. The addition of 1 per

cent. glucose improved the medium. The whole was covered with 1 cc. of liquid paraffin. The prepared culture medium was heated to 56°C. for one hour on three successive days.

Spirochaetes in this culture medium were found to be able to live and multiply over a wide range of temperatures. When the cultures were kept at 0°-12°C., they remained positive after eight months of daily examination, and even at 42°-45°C. the spirochaetes remained active though at higher temperatures they soon lost their virulence. They lived in cultures without passage up to a year but lost their pathogenicity at an early stage.

Spirochaetes from the severe cases lived longer in cultures than those from mild cases and first attack spirochaetes longer than those of a second attack. The solid and fluid parts of the medium also seemed to be of different importance and the solid part was found to harbour an invisible phase of the spirochaete. During the interval between two attacks all attempts to culture the organism from the patient's blood and bone marrow, liver, spleen and cerebrospinal fluid, were uniformly negative.

The cultures were found to exhibit a periodicity phenomenon, the spirochaetes disappearing and reappearing in the culture-tubes. The negative period ranged from 1 to 18 days the average being about 4 days. Simultaneous cultures usually relapsed at the same time or within a day or two of each other. There is a suggestion that the alternating immunological types also develop in cultures and that this property is independent of the antibodies of the host.

Rabbits and guinea-pigs were found to be naturally resistant to infection with this strain of *S. recurrens* but could be made relatively susceptible by blocking the reticulo-endothelial system by the injection of a suspension of carbon. Both mice and monkeys were susceptible but if the infective dose fell below about 0.5 cc. of the patient's blood, infection did not take place. The spirochaetes moreover were found to be less virulent towards the end of an attack.

The Addis Ababa strain was compared with a Debra Marcos strain which differed in the severity and mortality rate of the disease it provoked. The strains behaved rather differently in experimental animals yet the two are considered to be immunologically identical.

Lice were fed on relapsing fever patients and then kept at 37°C. and fed twice daily on the authors. Spirochaetes were continually present in the lice up to 18 days after being infected. A negative phase was not found. Neither the eggs nor the offspring of infected parents ever showed any signs of spirochaetes. Both the authors remained free from infection, thus confirming the well-known fact that the disease cannot be transmitted by the bite only of infected lice.

Relapsing fever spirochaetes were found to lose their infectivity to mice after an exposure of only 20 seconds to the ultraviolet rays of a Hanan quartz lamp at 32 cm. distance but remained motile up to an exposure of 10 minutes.

E. Hundle

PIROT R. & BOURGAIN M. L'infection latente résiduelle cérébrale chez le cobaye au cours des récurrentes à *Spirochaeta perniciosa*: la survie du spirochète dans l'encéphale est fonction de facteurs individuels. [The Latent Residual Brain Infection in Guinea-pigs Infected with *Spirochaeta perniciosa*: the Survival of Spirochaetes in the Brain is a Result of Individual Factors.] *Bull. Soc. Path. Exot.* 1945 v. 38 Nos. 1/2, 12-14.

The authors have infected guinea-pigs with a Peruvian strain of relapsing fever (*S. perniciosa*) by the bites of *Ornithodoros* and also by direct inoculation from one animal to another. Subsequently after varying intervals, the brains of guinea-pigs that had been infected were examined for residual infection by

inoculation into normal guineapigs. The results show that in some individuals spirochaetes may persist in the brain for at least 222 days whilst in others they disappear within 45 days. Moreover brain passage through a number of animals has no effect on the virulence of the spirochaete in guineapigs. The authors are of the opinion that in the case of *S. persica* the localization of spirochaetes in the brain is an unpredictable phenomenon which seems to depend on the individual susceptibility of the host.

E Hindle

PIROT R & BOURGAIN M. Perte du pouvoir infectant d *Ornithodoros tholozani* infecté congénitalement par *Spirochaeta persica* et surinfecté au stade nymphal. [The Loss of the Infective Power of *Ornithodoros tholozani* Congenitally Infected with *Spirochaeta persica* and Superinfected in the Nymphal Stage.] *Bull Soc Path Exot* 1945 v 38 Nos 3/4 88-90

The authors have maintained in the laboratory a strain of *Ornithodoros tholozani* supposed to be infected with *Spirochaeta persica*. Sixty first-stage nymphs which had hatched from eggs laid by infected parents and which proved infective were allowed to engorge on a guineapig whose blood was swarming with *S. persica*. About 3 years later the 26 ticks now adult which had survived failed to produce infection when fed on guineapigs and a few months later the 18 survivors also gave negative results when fed on another guineapig.

The results suggest that even in the same batch of young *Ornithodoros* all do not show the same susceptibility to infection with relapsing fever spirochaetes and also that infected ticks seem to die out more rapidly than those which remain free from infection. (See also E. HINDLE *Parasitology* 1911 v 4 133)

E Hindle

PIROT R. & BOURGAIN M. Résultats de la splénectomie chez le cobaye au cours de la récurrente à *Spirochaeta persica*. [The Results of Splenectomy in the Guinea-pig on the Course of Infection with *Spirochaeta persica*] *Bull Soc Path Exot* 1945 v 38 Nos 3/4 90-93

The authors removed the spleen from five guineapigs 55 to 149 days after inoculation with *S. persica* when the blood had been negative for spirochaetes for considerable periods. In no case did spirochaetes reappear in the circulation.

A sixth guineapig splenectomized whilst a few spirochaetes were still present in the blood became negative after 7 days without showing any multiplication of the organisms. Three of the splenectomized guineapigs were reinoculated subcutaneously with *S. persica* but did not become infected while three controls showed a heavy infection. It would appear therefore that in the guineapig removal of the spleen has no effect on the immunity following infection with *S. persica*.

E Hindle

CATTAN R. CORCOS A & COHEN H. La forme méningée de la fièvre récurrente. [The Meningitic Form of Relapsing Fever] *Bull et Mém Soc Méd Hôp de Paris* 1945 Nos 21 22 and 23 304-6

The authors have observed numerous cases of louse-borne relapsing fever at the Liberation Hospital Tunis. They also mention the existence of a widespread epidemic of this disease throughout Tunisia which broke out early in 1944 and had not ended at the time of their communication (June 29 1945). Clinical details are given of four cases showing simple meningitic forms of

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the disease all of which readily responded to treatment with novarsenobenzol. In addition two cases are added in which it was not quite possible to dissociate the symptoms from those of a chronic intoxication.

The authors suggest an analogy between relapsing fever and leptospirosis in both of which the liver may be affected, or meningitic symptoms develop and in both of which relapses usually occur. In view of the importance of the meninges in the development of syphilis meningotrophism would seem to be one of the more characteristic features of human spirochaetal infections.

E Hindle

WOLMAN M OMAR M & ABU TALEB M. Louse-borne Relapsing Fever treated with Calcium Gold Keratinate. *Lancet*. 1945 Dec. 15 775-7  
1 chart.

An account of the treatment of Egyptian patients infected with louse-borne relapsing fever carried out at the Imbaba Fever Hospital, Cairo.

The mortality of this epidemic averaged 2.6 per cent. but many of the patients had intercurrent diseases. A series of 100 patients whose blood contained spirochaetes and who also had pyrexia, were divided into two groups of 50 each. Patients in one group were given intravenous injections of 0.5 gm. neosalvarsan in 5 cc distilled water and those in the other group were left untreated. The drug caused frequent but mild reactions and no significant difference was found between those given 0.5 gm. neosalvarsan in water and a small group of patients not included in the above experiment, who were given 1.0 gm. neosalvarsan dissolved in water or calcium thiosulphate.

The injection of the drug caused the disappearance of spirochaetes within 24 hours in all cases and in most the temperature also came down within the same period and invariably within 30 hours.

In the treated group 17.5 per cent. had relapses and 5 per cent. non-specific rises in temperature the corresponding figures in the control group being 63.0 and 11.2 per cent. Moreover the mean length of interval between the attacks was significantly longer in the treated group. Three patients in the experimental group and one in the untreated group died of the infection.

E Hindle

HUTCHISON J H PIPPARD J S & GLEESON WHITE M H. SHEEHAN H. L. Outbreak of Weil's Disease in the British Army in Italy. Part I Clinical Study (HUTCHISON PIPPARD & GLEESON WHITE, *Brit Med J* 1946, Jan. 19 81-3 Part II. Post Mortem and Histological Findings (SHEEHAN) *Ibid* 83)

The description of an outbreak of Weil's disease among British soldiers in Italy who had all bathed in the River Arno or its tributaries, and in bomb craters during August and September 1944. There were 17 undoubted cases 5 fatal, all of which ran a similar course. The onset was sudden, with general weakness shivering and high fever nausea and sometimes vomiting. Severe headache was common though sometimes delayed, and general stiffness and aching developed during the next few days. The severe pain decreased when jaundice developed.

Intense conjunctival suffusion was constant and early in appearing. Icterus developed between the third and eighth days of illness and with one exception had a remarkable orange-yellow tint. The icterus persisted for weeks. Haemorrhages varying in degree were seen in every case. Visceral bleeding was common and was a factor in the death of the five fatal cases. A striking feature common to all cases was some degree of oliguria which in three of the fatal cases and two others became anuria for variable periods.

Treatment with penicillin 15 000 units 3-hourly up to a total of 600 000 to 660 000 units was tried in six cases. One patient died after receiving 210 000 units and there was no obvious effect on the course of the disease in the other five. Anti leptospiral serum was used in three cases also without any obvious beneficial effect.

Guinea-pigs were inoculated with blood (5 cc.) taken from 15 cases on the 3rd to 11th days of illness and two with 10 cc. of urine from two other cases on the 13th and 16th days respectively. Five of the animals died with typical symptoms of infection with Weil's disease and leptospires were grown from the kidneys of three of them. The blood of 13 of the patients was examined for agglutinins against local Cartwright strains or stock Wijnberg strains and all gave positive tests at a diagnostic level of 1/300.

Convalescence was slow in each of the 12 patients who recovered and they were not fit for discharge to a convalescent depot until 17 to 20 weeks from the onset of the disease. All except one showed anaemia which responded very slowly to iron therapy.

During the period when these men were in the wards over 1 800 cases of infective hepatitis were seen but only rarely did this disease simulate Weil's disease and the possibility of confusion between the two is remote. There were two doubtful cases thought to be enteric fever with jaundice until after recovery their blood was found to contain a rising titre of anti leptospiral agglutinins. Non-icteric leptospirosis may also have been present among some of the milder cases of P U O.

After the first cases were diagnosed an embargo was placed on unauthorized bathing etc. and the epidemic came to an end. At least two out of every ten rats caught in the neighbourhood were found to be carriers.

The post mortem and histological findings on six cases from this epidemic including the five referred to above are also described. The most characteristic features were prominent lesions in the kidneys involving cast obstruction and epithelial damage in the collecting tubules and also in the second convoluted tubules and the monocytic infiltration of the intermediate zone. There is said to be a close similarity between the appearances of the kidney in Weil's disease and in patients who died as a result of haemolytic transfusion reactions.

In every case brought to autopsy there was deep icterus of the skin and other tissues but the liver showed no obvious abnormality and microscopically there was never any trace of recent or healing necrosis nor of degeneration of the hepatic cells.

CURRENTS J. H. & WOODARD R. C. *Leptospirosis. Report of a Case from South Florida.* *Southern Med J* 1945 Dec. v 38 No 12, 811-13 1 fig [11 refs.]  
WEBER R. A. & FAVOUR, C. B. *Rat Bite Fever due to Streptobacillus moniliformis treated with Penicillin.* *Bull Johns Hopkins Hosp* 1945 Aug v 77 No 2 132-9 1 chart. [15 refs.]

The record of a typical case of rat bite fever due to *Streptobacillus moniliformis* which was cultured from the blood. In order to exclude a mixed infection with *Spirillum minus* a number of white mice were inoculated with the patient's blood and remained free from infection. On the 13th day of the disease when arthritic symptoms were at their height penicillin in doses of 8 000 units administered intramuscularly every two hours was started and continued for two days followed by 6 000 units every three hours for the next ten days. Blood cultures following treatment were negative and the arthritic symptoms gradually improved and disappeared within a month after the completion of treatment.



The patient has remained without any recurrence of symptoms for more than a year [See also this *Bulletin* 1945 v 42, 811]

The growth of *Streptobacillus* from the patient's blood was found to be inhibited by as little as 0.001 unit of penicillin per cc. in media which normally supported luxuriant growth.

E. Brindle

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## LEPROSY

CASARIAN T. Contagiousness of Leprosy. *Acta Med Orientalis (Palestine & Near East Med J)* 1945 June v 4 No. 6 181-4. [12 refs.]

The author gives information regarding the incidence of leprosy in Palestine and discusses the reasons for the low degree of contagiousness of this disease basing his remarks on 36 years' experience at the Jesus-Hill Leprosarium. None of the seven nursing sisters who worked at the institution for 13 to 33 years contracted the disease. Only 26 per cent of the leprosy patients admitted were known to have infected relatives and children of lepers brought up in a separate building did not develop the disease. The author states that every case of leprosy owes the infection to direct or indirect contact with another but that infection takes place only with difficulty owing to the low degree of virulence of Hansen's bacillus and that new infections are rare after the age of 30 to 35 years. During the last 70-75 years the number of cases in Palestine has fallen from 220-250 to 120-150.

L. Rogers

DEGOTTE, J. Nouvelle contribution à l'épidémiologie de la lèpre. Étude comparative de la chefferie de Makoda 1939-1943 [The Epidemiology of Leprosy—a Comparative Study in 1939 and 1943 in Makoda.] *Rec Travaux Sci Méd Congo Belges* 1945 July No. 4 70-81 3 maps & 1 graph.

This paper reports on a comparative study of the incidence of leprosy in 1939 and 1943 in a north-western area of the Belgian Congo the mean altitude which is 800 metres. It consists mostly of grassland, with comparatively leprosy incidence and some forest areas with higher rates. In 1939 15,528 and in 1943 16,106 of the inhabitants were examined, and infection rates of 4.33 and 4.25 per cent respectively were found indicating a slight decline in the disease. The incidence in different divisions of the area examined varied from 2 to 6 per cent. The number of new cases found in 1943 amounted to 210 the highest incidence being found in persons aged 30-40 there was also a high rate among a few persons over 60. A table is given of cases classified according to the Cairo Conference system. It is stated that the majority of the lepromatous cases have been effectively segregated, and the author deduces that the occurrence of about as many new cases in the area under observation during the four years under consideration as for leprosy in general proves that neural leprosy is contagious. [If the segregation of the infective cases was carried out at or about 1939 the occurrence of a number of new cases during the next four years may largely be the result of infections which took place before the infective cases were segregated—the incubation, or latent period of leprosy is often of several years duration before the first symptoms appear.]

L. Rogers.

TROUT C. L. Agglutination Test with the Leprosy Bacillus. *J Trop Med & Hyg* 1945 Aug Sept. v 48 No 4 73-4

In this short note the results are reported of the use of an antigen prepared from cultures of a pleomorphic acid fast bacillus obtained in California called the Rethi bacillus and one prepared from *Mycobacterium leprae* separated from lepromata. One vaccine contained a toxin filtrate taken from a milk culture of the Rethi organism and a second a similar substance from a broth culture. Sera taken from ten persons vaccinated with these products in 1 cc. doses weekly for six doses agglutinated leprosy bacilli taken from lepromata. Attempts were therefore made to immunize the children of lepers and others who had associated with lepers by means of these vaccines which produced temperatures as high as 103 F in control patients but seldom a rise above 100°F in lepers. The Rethi vaccines sterilized by 1 per cent formalin were also used for treatment in a group of lepers and the author has the impression that the milk culture toxin-filtrate was the more effective both for treatment and prophylaxis but it is too soon to form conclusions

L. Rogers

CHORINE \ Nouvelle réaction de floculation de la lèpre [A New Flocculation Reaction in Leprosy] *Méd Trop* Marseille. 1943 Nov Dec. v 3 No 6 419-48 5 graphs [13 refs] Also in *Ann. Inst Pasteur* 1944 Sept Oct & Nov-Dec. v 70 Nos 9/10 & 11/12 257-76 341-56 5 graphs [13 refs]

These two references refer to the same paper. It gives full details of a comprehensive investigation of a flocculation reaction of diagnostic value on the lines of the Rubano reaction which consists in the sedimentation of formalized red corpuscles of the sheep and of Westergren's measurements of the rapidity of sedimentation of non formalized red corpuscles. Formalized red cells sediment more quickly than unformalized cells in the presence of the serum of a leprosy subject. Chorine has sought to isolate the active principle of formalized cells by preparing extracts of formalized blood or tissues and using the extract as an antigen. After trying a number of chemicals he found that 90 per cent alcohol was the best solvent of the antigen for full details of the preparation of which the original paper should be consulted by those interested in its use.

In using this test 1 cc. of the antigen is poured into 2 cc. of double distilled water and mixed at a speed of 200 revolutions per minute at the end of which 8 cc. of distilled water are added. The optical density is measured by photometry and the reaction is calculated as the difference between the degree of density found for the curve of an emulsion with the serum to be tested and that of a mixture with distilled water only. A series of tubes is put up with increasing proportions of the serum and decreasing proportions of antigen to allow curves to be plotted. A series of illustrative curves under different conditions of the numerous experiments is given in the paper from which the following conclusions are derived. The sera to be tested should be heated for 30 minutes at 55 C. The reactions should be carried out at a temperature of 25°C for 4 hours this may necessitate a cooling apparatus when working in the tropics. The antigen is best used in a dilution of 1 in 10 and within half an hour of the preparations of suspensions of it. The sera should be kept before use at a temperature of 4°C at which they can be kept for 4 or 5 days. Three series of four tubes each are put up. In the 4 tubes of the first series 0.15 cc. serum in the second series 0.20 and in the third series 0.50 cc. are placed. In each of these series the first two tubes are filled up to 1 cc. with the suspension of the antigen. The remaining two tubes are filled up to 1 cc.

with alcoholized water these are control tubes. They are mixed well and kept at a temperature of 25°C. for four hours before the densities of the flocculation are read. The result of the reaction is obtained by subtracting the photometric degree of the control tube from that of the reaction tube.

Tables are given of the data obtained in 200 cases of leprosy and in 100 controls. A difference of over 30 in the densities between the control tubes and those showing the reaction of leprosy sera is considered to be a positive reaction for only 6 of the 100 controls gave figures up to 30-35 and 2 of 35-40. On the other hand only 10.5 per cent. of leprosy sera gave figures below 30 and in 21 the figure exceeded 200. Feeble reactions indicated by figures of 30-35 numbered only 18.5 per cent. and very intense reactions of over 100 also numbered 18.5 per cent. The low reactions were chiefly met with in slightly affected or stationary cases and in those which had much improved under treatment. High figures occurred during lepra reactions and in advanced cases with nodules. In general tuberculous cases gave low degrees of reaction as compared with lepromatous cases. This new reaction thus appears to be of both diagnostic and prognostic value.

L. Rogers

FLOCH H. & DE LAJUDIE P. Sur la lèpre et les intradermo-réactions à la lépromine (Mitsuda) et à la léproline (Souza Aranjó) en Guyane Française. [The Intradermal Reactions to Lepromine and Leproline in Leprosy in French Guiana.] *Institut Pasteur de la Guyane et du Territoire de l'Inini* Publication No 97 1945 Jan. 15 pp. [24 refs.]

The authors have used both leprolin, supplied by Professor de Souza Aranjó and lepromin prepared by the method of Hayashi in their tests on 88 cases of leprosy. Positive Mitsuda reactions were obtained in 90 per cent. of tuberculoid, in 51 per cent. of nerve in 9 per cent. of mixed cases but in none of 10 lepromatous patients. In controls not infected with leprosy reactions were negative in those aged 8 to 9 years but positive in four of eight persons aged 10 to 14 years. With the use of the Souza Aranjó's leprolin, similar results were obtained in lepromatous and mixed cases but in only 27 and 23 per cent. respectively in tuberculoid and nerve cases.

L. Rogers.

TAYLOR, C. E. Leprosy of the Large Intestine and Gall-Bladder. Case Report with Review of the Literature. *Trans Roy Soc Trop Med. & Hyg* 1945 Oct. v 39 No 2, 125-32, 5 figs. on 2 pls. [17 refs.]

The author points out that the gastrointestinal and biliary tracts are among the few parts of the body generally supposed to escape involvement in leprosy but they now report changes in these tissues in a fatal lepromatous case in a West Indian Negro with both skin and nerve lesions. The gall-bladder showed a thickened mucosa with a mosaic pattern due to thickened patches which, on section, revealed a few leprosy bacilli. Similarly the large intestine showed thickening of the mucous membrane with large ulcers in the lower portions and smaller ulcers in the upper parts, in the inflamed and oedematous margins of which both scattered and clustered acid-fast lepra-like bacilli were found. The patient had died during an active lepra reaction accompanied by diarrhoea. The macroscopic and microscopic characters of the lesions are illustrated.

L. Rogers.

MONTEL, R. & BASSET. Deux cas d'infantisme lépreux. [Two Cases of Leprotic Infantilism.] *Bull. Soc. Path Exot* 1944, v 37 Nos 11/12, 332-7 3 figs.

AGENT G. H. & POGGE R. C. The Therapeutic Effect of Promin in Leprosy  
*Pub Health Rep* Wash. 1945 Oct 5 v 60 No 40 1165-71 8 figs on 2 pls

This paper records further trials of promin in leprosy in continuation of those reported in November 1943 [this *Bulletin* 1944 v 41 494].  
 The present report is based on the treatment of 137 patients at the U.S.A. National Leprosarium by means of 32 000 intravenous injections amounting to a total of 128 961 gm. The average daily dose including days of rest varied from 0.4 gm. to 4.6 gm. The usual dosage is 1 gm. daily increasing to 5 gm. but in some patients who showed toxic reactions the maximum daily dose did not exceed 2 gm. The present routine consists of 2 to 5 gm. daily by the intravenous route on six days each week in courses up to two weeks with a week's rest between the courses which allows of restoration of the red corpuscles lost during a course. The longer the duration of the treatment and the larger the doses the greater the benefits as shown by tables of data. The percentage of the total 137 patients treated who improved was 58.4 the figures for treatment of less than six months and for more than six months respectively being 25.6 and 71.4 per cent. All of six cases treated for 3 to 4 years had improved. A total dosage of less than 500 gm. only produced improvement in 25.6 per cent. but with 500 to 1 000 gm. the percentage rose to 72.5 per cent. or nearly three-fourths of the patients. Only two patients became worse while under treatment both were advanced cases with involvement of the larynx. The improvement was objective and not only subjective this is confirmed by photographs of patients with advanced lepromatous disease before and after treatment the benefits are not limited to action against secondary infections. In over 10 per cent. of 62 patients treated for more than one year positive bacteriological findings have changed to negative on several consecutive monthly examinations. Serological reactions may also become negative coincidentally with improvement in or arrest of the disease as shown by tables of data. The cost of the drug is not given. Promin is not claimed to be a specific remedy for leprosy but there is evidence that it has at least an inhibitory effect on the progress of the disease and that it even causes retrogression in some lesions. There is therefore some hope that continued chemotherapeutic research may produce a still more effective remedy. Preliminary studies suggest that diarsone has a similar action to promin and that it may prove even more effective.

L Rogers

GUICHARD F Préparation directe en partant des graines des esters d *Hydnocarpus anthelmintica* Pierre en vue du traitement de la lèpre [Préparation of Esters of *H. anthelmintica*.] *Bull Soc. Path. Exot* 1945 v 38 Nos 1/2 9-12

The author points out that most methods of preparing the soaps and ethyl esters of the fatty acids contained in the oils used in the treatment of leprosy are laborious and he describes a simpler method in which the fatty acids contained in the seeds are dissolved without transformation in an apparatus containing absolute alcohol and sulphuric acid. The seeds are sterilized in an autoclave and decorticated. The kernels are scorched, kept at 100°-110°C. for a night before being pulped, and are then mixed with one third of their weight of sandstone in fine grains to facilitate the penetration of absolute alcohol to which 5 gm. sulphuric acid per 100 cc. has previously been added. The amount of acid-alcohol is equal to the weight of the pulped kernels. Some grains of pumice-stone are added and heat is applied. The results of distillation are collected over a period of ten hours. The products are treated with 15 per cent. chlorinated water several times washed twice with distilled water and neutralized with a

small quantity of anhydrous sodium carbonate to purify the esters. To preserve them 2 gm. per cent. of anhydrous sulphate of soda is added to each full well-corked container. Before placing in ampoules 1 per cent. gulacol is added and the ampoules are sterilized at 115 C. for 15 minutes. The esters thus prepared keep well and are well borne by the patients. L. Rogers.

MONTEL, R. La méthode de Charpy dans le traitement de la lèpre. [The Treatment of Leprosy by Charpy's Method.] *Bull. Soc. Path. Exot.* 1945 v 38 Nos 3/4 63-4

Charpy's method of treating lupus is as follows: vitamin D 15 mgm. three times during the first week of treatment; twice a week during the next three weeks; and once a week during the next four months; calcium gluconate by intravenous injection of medium doses three times a week, and a litre of milk daily are given for the same period. The author has tried this treatment in two cases of leprosy.

One patient suffering from nodular leprosy and already much improved by treatment with methylene blue and chaulmoogra, showed considerable further improvement under the Charpy method: the paratuberculous monocytes decreased in number; the lepromata and lepromatous infiltrations diminished markedly in size and the patient's bodily state improved.

The other patient suffering from trophoneurotic leprosy showed remarkable improvement in his general condition: increase of weight and decrease of nerve pains.

The author thinks that these results are encouraging and that further trials of the method should be made. J. F. Corson

## HELMINTHIASIS.

ALVES W. & BLAIR, D. M. Schistosomiasis. Intensive Treatment with Antimony. *Lancet.* 1946 Jan. 5 9-12.

In a preliminary communication one of the authors [this *Bulletin* 1945 v 20 815] has already recorded the satisfactory result of rapid intensive treatment of schistosomiasis with antimony. In this paper the authors record in more detail similar treatment of 100 cases of *S. haematobium* and *S. mansoni* infections chiefly in African soldiers. Basing their investigations on the work of CHARGES and his collaborators (*J. Amer. Med. Ass.* 1935 v 104 878) which led to the intensive arsenical therapy of syphilis with intravenous drip transfusion (HYMAN *et al.* *ibid.*, 1939 v 113 1208) [see also *Bulletin of Hygiene* 1940 v 15 234] and later to the therapeutically more effective "multiple syringe injections" (EAGLE and HOGAN quoted by COLE *et al.* *Bulletin of Hygiene* 1944 v 19 104) the authors found that continuous intravenous injections of 100 cc. of a 1 per cent. solution of sodium antimonyl tartrate in 5 per cent. glucose-saline caused excruciating phlebalgia. They abandoned this technique for the multiple syringe method, giving intravenous injections three times daily at three-hour intervals for two days—a total of six injections, given at 9 a.m., 12 noon and 3 p.m. on each of two consecutive days. The preparation of antimony employed was sodium antimonyl tartrate and the amount of drug injected at each dose was usually 1 grain or 2 grains.

Each injection was made in 10 cc. of 5 per cent. glucose saline into a vein in the antecubital fossa and given steadily at a rate not exceeding 2 cc. per minute. At least five minutes were therefore taken for each injection, and the

authors stress the point that *This slow and steady injection of the drug is of fundamental importance in the success of the treatment*. In no case have toxic reactions led to interruption or discontinuance of the course and the absence of the more troublesome manifestations usually associated with the intravenous administration of antimony was striking. Cough resulted in only 16 of the 100 cases during or more commonly after the first injection and never lasted more than two minutes. The frequency of its occurrence diminished through the course and only two patients suffered from it as a result of their sixth and final injection. Vomiting did not occur in association with the second but was encountered in six cases and two cases respectively with the fifth and sixth injections. In the 100 cases a feeling of constriction of the chest was noted by one asthmatic patient only. Abdominal cramps occurred in three cases there were no rheumatic pains and no collapses. Salivation was common after the early injections but usually vanished by the second day. The average rate and the regularity of the pulse in the whole series was not altered by the antimony dosage. In two cases there was a brisk haematuria after the third injection but in neither did it persist. In one there was a drug rash of limited distribution appearing 24 hours after the last injection and persisting for one week. A striking feature in many cases was a state of euphoria the day after the conclusion of treatment. This could not be ascribed to relief as the African does not as a rule fear injection treatment and it was noticed both in Europeans and in Africans.

Data relevant to the 100 cases treated are listed in tabular form showing the species of parasite the degree of eosinophilia, the patient's weight in pounds and the gross dosage of S.A.T. given to each. This gross dosage ranged from 7 grains to 14 grains of S.A.T. and is based on the body weight. A man of 144 grain of S.A.T. being given for each 12 pounds of body weight. The individual doses six for each individual were worked out for the sake of economy and convenience so that as often as possible 1 grain or 2 grains were given. For example (doses in grains) —

	9 a.m.	12 noon	3 p.m.	9 a.m.	12 noon	3 p.m.
Patient A gr 10 S.A.T. given as	2	2	1	2	2	1
Patient B gr 13½ S.A.T. given as	2	2	2½	2½	2½	2
Patient C gr 9½ S.A.T. given as	2	2	1	2	1½	1

The authors record their use of an intradermal test in diagnosis. The test was performed with a cercarial antigen and its development and application are to be described in another communication. This test was used in initial diagnosis which was confirmed in each case by the examination of urine and of stools for schistosome ova. The skin test had become negative in a big proportion of the cases retested two months after treatment and where this reversion took place the authors regard it as indisputable evidence of the death and dissolution of the worms. In none of the 100 cases treated were schistosome ova found in the stools or in the urine two months after treatment. Of the 53 cases re-examined two months after treatment only 14 gave a positive skin test. Nine of these 14 were retested one month later six of them had then become negative two remained positive and one originally strongly positive had become only weakly positive. In no case examined two months after treatment were eggs found in the excreta.

In eight cases the urinary antimony excretion was estimated during the course of treatment and for 24 hours afterwards. Data are given in a table showing that between 70 and 80 per cent. (in the average case of this series 8 grains of S.A.T.) of the antimony injected remains in the body 72 hours after beginning treatment and this high concentration of antimony in the body is held by the authors to be responsible for the rapid disappearance of ova and the apparent cure of all their cases.

The authors discuss the obvious economic and public health advantages inherent in their short intensive course of treatment for schistosomiasis and point out its manifold implications in the mass treatment of the populations inhabiting the highly endemic areas of the world. They suggest that intensive antimony therapy may find a place in the treatment of kala-azar, other forms of leishmaniasis and filariasis.

[This important paper may well open a new chapter in the treatment, with the heavy metals, of protozoal and of helminth infections.]

A. R. D. Adams.

MILLS W. G. Treatment of Schistosomiasis. *Lancet* 1946 Jan. 5 12-13.

The author treated 46 cases of *S. haematobium* infestation in West African native troops with daily intramuscular injections of Stibophen (B. W. & Co.) [=Fouadin, Bayer] or of Anthiomaline (M. & B) for 6 days during each of two successive weeks. He either "cured" or "presumably cured" all but four of the 46 cases. Where he claims cure the bladder was free from all tubercles, ulcers and granulations on monthly cystoscopy for three months after treatment. Presumably cured cases showed cystoscopically a virtually normal bladder on the occasions on which it could be examined, and no clinical relapse was reported. Toxic complications of treatment with either drug were minimal, and vanished, where present, within a week of ending treatment.

In the four uncured cases two developed new crops of tubercles in the bladder within three months of treatment: one had a small contracted bladder and had to be invalided from the army and the last had a severe chronic and relapsing staphylococcal cystitis which also led to his being invalided. The author draws attention to the possibility of late relapses but considers these improbable in his series of cases. He stresses the importance of cystoscopic control throughout the treatment of urinary schistosomiasis.

A. R. D. Adams.

WARD R. O. Some Surgical Aspects of Urinary Bilharziasis. *Proc. Roy. Soc. Med.* 1945 Nov. v. 39 No. 1 27-38 (Sect. of Urology 1-12) 23 figs. (12 coloured)

This paper presented to the Urological Section of the Society contains a general account of urinary schistosomiasis from the standpoint of a urological surgeon. It contains nothing new and is designed to direct attention to the possible occurrence of schistosomiasis in members of the forces who have served overseas during the recent war. The author stresses the value of cystoscopic examination which may reveal the diagnosis in the apparent absence of cells and of ova from the urine.

A. R. D. Adams.

PETERS, C. N. HUNTRESS R. L. & PORTER, J. E. Urinary Schistosomiasis. Report of Two Cases in Malina. *J. Urology* 1945 Sept. v. 54, No. 3 301-6, 3 figs.

OLIVER GONZÁLEZ J BIAGGI N & RIVERA LEÓN J The Effect of Chlorine on the Motility and Infectivity of the Cercariae of *Schistosoma mansoni* Puerto Rico J Pub Health & Trop Med 1945 Mar \ 20 No 3 357-61 [Spanish version 362-6]

The authors investigated the question as to whether the inactivity of cercariae of *S. mansoni* after exposure to chlorine (calcium hypochlorite) also implies their loss of infectivity. They found that chlorine concentrations of 1.25 to 0.5 parts per million parts of water caused the cercariae to become inactive in the average times of 2.5 to 10.4 minutes but that a concentration of 0.2 part per million had no definite effect. In the infectivity tests rats were exposed for one hour to the cercariae as soon as the latter were observed to be completely inactive. Concentrations of chlorine of 1.25 parts per million for a maximum duration of exposure of four minutes or 0.44 part per million for 18 minutes made the cercariae inactive and non infective. A concentration of 0.22 part per million did not exert a sure effect on the motility of the cercariae and those that apparently showed inactivity at this concentration were still infective to rats.

It is suggested that a minimum period of exposure of 20 minutes to the effects of a chlorine solution yielding a minimum chlorine residual of 0.50 part per million of water may be sufficient to render cercariae of *S. mansoni* non infective.

J J C Buckler

WELLER T H & DAMMIN G J The Acid-Ether Centrifugation and the Zinc Sulfate Flotation Techniques as Methods for the Recovery of the Eggs of *Schistosoma mansoni* Amer J Trop Med 1945 July \ 23 No 4 367-74 1 fig [17 refs]

The authors carried out studies designed to evaluate and compare the effectiveness of the acid-ether centrifugation and the zinc sulphate flotation techniques in the recovery of eggs of *Schistosoma mansoni*.

Uniform suspensions were prepared of 48 faecal specimens each containing relatively large numbers of *S. mansoni* eggs. 25 were found to contain more than 400 eggs per cc. by the Stoll count. The suspensions were employed in testing the efficiency of four different techniques. Calculations of the percentage recovery of available eggs were limited to the group of 25 suspensions containing more than 400 eggs per cc.

(1) *Acid-ether routine technique*—One cc. of the suspension and 5 cc. of 40 per cent HCl (40 cc. conc. HCl diluted to 100 cc.) are mixed by shaking in a 15 cc. centrifuge tube filtered through two layers of moist gauze and then mixed with an equal quantity of ether. The mixture is shaken thoroughly and spun for 1 minute at 1500 r.p.m. The mixture is shaken thoroughly, junction is loosened and then the acid and ether layers are poured off and discarded, leaving a few drops of the egg bearing sediment which is decanted on to a slide for egg counting.

(2) *Zinc sulphate flotation with loop removal*—Using 1 cc. of the basic suspension this method is essentially similar to that outlined by FAUST *et al* [this Bulletin 1940 \ 37 62]

(3) *Acid-ether semi-quantitative technique*—This method follows that of (1) up to and through the centrifugation step. Thereafter the ether and acid layers together with the floating debris are removed by pipette and discarded leaving 1 cc. of the acid and sediment. The latter are mixed together and three samples of 0.075 cc. each are withdrawn and prepared for egg-counting. The results of six counts are averaged and the number of eggs per cc. of undiluted faeces is calculated.



JAFFÉ, R. Observaciones sobre lesiones pulmonares producidas por *Schistosoma mansoni* (Su frecuencia y su importancia.) [The Frequency and Importance of Pulmonary Lesions in *Schistosomiasis mansoni*] *Rev. Sanidad y Asistencia Social* Caracas, 1944 Dec. v 9 No 6 1287-88. [13 refs.]

Pulmonary schistosomiasis i.e. lesions due to the presence of ova of *S. mansoni* in the lungs is far from uncommon—the author found them in 12 out of 50 cases examined—but only rarely (2 per cent. of autopsies) are the lesions extensive enough to produce changes visible to the unaided eye. SHAW & GHARIB have noted them in 33 per cent. of cases in Egypt and KOPFISCH in 64 per cent. of 147 examined in Porto Rico. Dew thinks that this condition is more common in infestations by *S. haematobium* than in those by *S. mansoni*.

Four questions arise from this association: (i) In what proportion of cases of schistosomiasis do we find this pulmonary involvement? As stated above the author found it in 12 out of 50. (ii) How often are these lesions the result of the presence of the worms or their ova extensive enough to cause confusion with other diseases such as tuberculosis? This is not answered, as data are insufficient. If the nodules are few the chances of this confusion arising are slight but if grouped, as they sometimes are they may cause confusion unless more detailed investigation is made. (iii) Is there evidence of involvement of organs other than the lungs in these cases? Yes the ova may be seen in the portal radicles and the parasites and their ova in the liver and elsewhere. (iv) Is there any connexion between pulmonary schistosomiasis and tuberculosis of the lungs in the sense that either predisposes to the other? The author arrives at a negative conclusion, finding that tuberculosis is no more common in schistosomiasis patients than in the general population. The tubercles found in schistosomiasis do not contain any *Mycobacterium tuberculosis* and are "pseudo-tubercles" unless the word is used purely generically.

Apart from these considerations the lesions may be so extensive as to give rise to chronic interstitial pneumonia if sparse not enough to cause any serious symptoms but, if widespread, enough to cause secondary cardiac embarrassment [see this *Bulletin* 1938 v 35 665].

In conclusion the author is of the opinion that these pulmonary lesions of schistosomiasis have as a rule little if any importance and are rarely sufficiently serious or widespread to cause symptoms but at the same time when radiological examination of the lungs shows small scattered nodules the possibility of schistosomiasis pulmonum should be borne in mind. *H. Harold Scott.*

BANG F. FERGUSON M. S. HAIRSTON N. G. & GRAHAM, O. H. Hyperendemicity of *Schistosoma japonicum* on Leyte Island, P.I. *Amer. J. Trop. Med.* 1945 Sept. v 25 No 5 407.

Ova of *Schistosoma japonicum* were found in the faeces of 80 per cent. of native children over 10 years old in the eastern side of the island of Leyte in the Philippine Islands—on only a single examination, followed if negative by a second examination after sedimentation of a portion of the faeces was made in each case, the authors infer that everyone in the endemic areas becomes infested before reaching the age of 15 years. The incidence was less in adults than in children, the difference being statistically significant and this suggests that immunity may be developed. *J. F. Connor.*

MAGATH T. B. & MATHIESON D. R. Infection of Wild Rats on Leyte with *Schistosoma japonicum*. *U.S. Nav. Med. Bull.* 1945 Dec. v 45 No 6 1195-202.

It is well known that the endemic area of human infestation with *Schistosoma japonicum* on Leyte Island in the Philippine Islands is limited to the

Leyte Valley which is about 25 miles long and 8 miles wide and is situated on the east side of the island.

Wild rats in this island appear not to migrate much but to remain throughout their lives in one relatively small area. It was thought therefore that an investigation of the incidence of infestation in these rats might give more information in relation to certain bodies of water and to the distribution of the small *Schistosomophora quadrax* than the examination of man and his domestic animals would, especially in the disturbed conditions caused by the war.

Rats were trapped in various localities 163 altogether being caught. They comprised Polynesian rats (10) Norway rats (14) and Black rats (139) the subspecies being undetermined. They were caught in the following places (the numbers infested are shown in brackets): Santa Fé Tacloban 58 (0) Palo 43 (11) Gacac 41 (37) Dagami 7 (4) Infested rats always had eggs in the posterior central lobe of the liver and Antonio Samar 6 (0) Jinamoc Island 2 (0) Total 163 (84) next in frequency were eggs found in the faeces and the authors suggest that the blood vessels of the rat's intestine are too narrow for the female worm to enter so there is insufficient pressure to force the eggs through the bowel wall. The authors conclude that the wild rat is not important for the spread of the disease but that it might be used to define a limited area in which *S. japonicum* is being spread and that the proportions infested might indicate the intensity of infestation of other hosts in the area.

JOHNSON A. S. Jr & BERRY V. G. *Axiatic Schistosomiasis* Clinical Features, Sigmoidoscopy Picture and Treatment of Early Infections. War Medicine Chicago 1945 Sept. 8 No 3 150-62 5 figs. J. F. Corson

*Schistosoma japonicum* infestation of man occurs in China Japan Formosa the Celebes and the southern Philippine islands of Mindanao Samar and Leyte. The authors record their observations on and treatment of a group of 42 cases in the last named island admitted to the station hospital in the early stages of the disease. In all these patients exposure to probably infected water. In four cases the duration of previous exposure to the finding of eggs in the stools was determined as 30 35 40 and 44 days respectively. In the 38 others it ranged from 30 to 71 days before the manifestation of symptoms. The only constant physical sign was a tender palpable liver. The investigations they made in their cases and the investigations they made in their cases and biopsies of the distinctive moldoscopically in 67 per cent of their cases and particularly at the recto-sigmoid junction revealed ova. The lesions are so characteristic that routine biopsy is unnecessary. Twenty two patients were treated with the usual course of potassium ammonium tartrate and 20 with Fouadin. The former gave rise to the usual side effects the latter to none. The cure rates have not yet been established, but therapy resulted in clinical improvement a fall in the average eosinophil count and the disappearance of ova from the stools.

LARRH J. E. Jr Effects of Alcohol on Natural Resistance to the Dwarf Tapeworm in Mice 1945 Oct. 31 No 5 291-300 [16 refs.] A. R. D. Adams

BARNETT L. Progress in our Knowledge of Hydatid Disease. With some Contributions thereto from the Otago Medical School. *New Zealand Med J* 1945 Dec. v 44 No. 244 304-8 2 figs.

An interesting summary of work on hydatids by the Chairman of the Hydatid Research Committee. He stresses the fact not sufficiently recognized, that primary peritoneal cysts are rare less than 1 per cent. of the whole they are nearly always secondary to cyst of the liver which has escaped notice for cysts of the dome of the liver may grow slowly for 30 years or even longer before producing signs of ill-health. Also the vast majority of primary cysts arise in childhood, and the aphorism that "a hydatid cyst is nearly as old as its host" is generally true. Biliary colic and jaundice may be caused by a cyst opening into the bile-ducts this is not rare and in hydatid countries should always be borne in mind.

The author makes some observations on operative details indicating his preference for the abdominal rather than the lower thoracic route for cysts of the dome, for these cysts are usually old and degenerated and contamination and sepsis occur twice as frequently after transthoracic as after the abdominal operation.

Lung cysts in the young should be given the chance of spontaneous cure unless there are indications of sepsis and toxæmia. The danger of tapping is duly noted. [The abstractor had a sad experience of this more than 50 years ago when as house physician, he was directed to aspirate a "pleural effusion". When the aspirator was thrust in the patient died in a few seconds drowned in the fluid the cyst-wall had ripped up and the lung was flooded with the fluid which autopsy showed to be hydatid.] Brain cysts when primary nearly always occur in childhood if in an adult a brain cyst is probably secondary to cyst of the heart.

Study of the hexacanth embryo leads the author to conclude that the central pair of spirules is used for penetration of tissues and the lateral pairs for propulsion. The size of the embryo has been variously recorded the author finds it to be 28 $\mu$  long by 25 $\mu$  broad, and the whole ovum 41 by 34 $\mu$ . Again, contrary to the fairly general idea that the gastric juice of the host acts on the egg-shell to liberate the embryo he believes (with DÉVÉ and others) that hatching takes place in the small intestine where the contents are alkaline.

There is probably a high degree of innate immunity in dogs to hydatid infection, otherwise infection would be much more prevalent than it is at the same time if experiments now in hand succeed and immunity can be artificially conferred on dogs and lambs this will go a very long way towards the control of hydatid in the country  
H Harold Scott

DESCHIEUX, R. L'action anthelminthique des colorants triphénylméthaniques. [Anthelmintic Action of Triphenylmethane Dyes.] *Bull Soc. Path. Exot.* 1944 v 37 Nos. 3,4, 111-25 [10 refs.]

DESCHIEUX, R. & LAMY L. Données expérimentales et pratiques sur les propriétés anthelminthiques de la phénothiazine (thiodiphenylamine) et de ses dérivés. [The Anthelmintic Properties of Phenothiazine and its Derivatives.] *Bull Soc. Path. Exot.* 1945, v 38 Nos. 9 10 288-89. [22 refs.]

FLOCH H. & DE LAJUDIE P. Sur la filariose à *W. bancrofti* en Guyane Française, la lymphangite endémique et l'éléphantiasis des pays chauds. [Filariasis due to *Wuchereria bancrofti* in French Guiana. Endemic Lymphangitis and Elephantiasis of the Tropics.] *Institut Pasteur de la Guyane et du Territoire de l'Inini Publication No 109* 1945 Aug. 17 pp. [23 refs.]

Thick blood films taken from the finger at 3 p.m. and between 9 and 10 p.m. from natives of French Guiana and others were stained with Giemsa's stain and

examined for microfilariae. These were present in 27 (12.4 per cent.) of 217 males and 20 (18.1 per cent.) of 110 females. In cases where a specific diagnosis was difficult the microfilariae were identified by measurement all were diagnosed as of the species *Wuchereria bancrofti*. The authors have not found the embryos of *Filaria azardi* (*demarguayi*) or *Acanthocheilonema perlati* in natives of French Guiana.

The aetiology of tropical lymphangitis and elephantiasis is discussed and the authors subscribe to the view that they are caused by streptococcal infection.

RIFEHN H & THOMPSON K J. Structural Changes in Early Filariasis. *Arch Pathology* 1945 Oct. v 40 No 4 220-24 5 figs

This account is based on a study of 30 cases. Some of the patients had been stationed in South Pacific islands where filariasis is endemic. Others showed signs leading to suspicion of filarial infestation. Eighteen of them had blood eosinophilia of 6-11 per cent. in others the percentage did not exceed the normal and the total red and white counts were within normal limits. No organisms such as streptococci were found in any of the lesions. In most the first symptoms were a painful enlarged lymph node a brawny lymphangitis or an acute epididymo-funiculitis. In 12 the genitalia or lower limbs were primarily involved in 9 the upper limb and in 9 the upper and lower limbs at the same time. Presence of the filaria was demonstrated in 6 of the patients in the others though the worms were not found the histological picture was to all intents and purposes the same.

The essential changes comprised marked hyperplasia of the related lymph follicles with mitotic figures at the germinal centres and general infiltration with eosinophilia. The lymphatic channels showed fluid lakes of the pink-staining albuminoid fluid. The histological changes were dilatation of the lumen of the lymphatics with necrotic debris thickening of the wall and eosinophilic infiltration with epithelioid cells fibroblasts and multinucleated cells of the Langhans type. Three cases are detailed—in men of 23, 25 and 29 years respectively—and a plate of six photomicrographs illustrates these changes so far as uncoloured photographs can do so.

The author summarizes the changes in these words: There appear to be three stages in the genesis of filariasis (i.e. the local tissue reaction to infestation) first the acute stage manifested by a typical allergic reaction which may be local or systemic second the subacute or early chronic stage characterized by the development of a proliferative granulation tissue and occurring in lymphatic tissues harboring the parasite third the late chronic stage of the disease typified by a non specific fibrous tissue overgrowth. As in all classifications no distinct delineation is possible. One stage merges imperceptibly into the other.

It is noteworthy that a large proportion of the patients became infested without presenting any symptoms at all events any at present recognizable.

DEHAYAGUDE R. G. Microfilarial Granuloma of the Spleen. *Observations in Twelve Additional Cases*. *Arch Pathology* 1945 Oct. v 40 No 4 275-8 8 figs on 1 pl.

This article may be regarded as confirmatory or supplementary to that published in 1942 by the author and B. M. AMIN on the same subject [see this *Bulletin* 1942 v 39 707] in which 11 such cases are considered. The present record brings the total to 23. Taking all together the ages of the subjects ranged from 6 to 70 years but 20 were between 25 and 50 years. 5 were females (111).

18 were males. In 10 of the present series however living specimens of microfilariæ were obtained from the splenic granulomata whereas in the previous 11 the description was made from fixed tissues. Obtaining them alive has enabled a definite diagnosis of *B. bancrofti* to be made. Prior to this there had been a suspicion that it might be the Malayan filaria. Even when microfilariæ are not seen the histological structure is the same (except that the lymphocytes eosinophiles and giant cells of early granulomatous reaction had disappeared) and represented a later fibrosed condition of a granulomatous lesion. The macroscopic features the author avers are so definite that mere inspection enables one to say that the lesion is of microfilariæ genesis.

H Harold Scott.

See also p 295 COGGESHALL L. T. Malaria and Filariasis in the Returning Serviceman.

CULBERTSON J. T. ROSE H. M. & OLIVER-GONZALEZ, J. The Chemotherapy of Human Filariasis by the Administration of Neostibosan. Second Report. *Amer J Trop Med.* 1945 Sept v 23 No 5 403-8

*Bancroftian filariasis* although it has proved a smaller military problem than was expected is widespread in the native populations of certain areas. Measures of protection adequate for military personnel are inadequate for civilian communities. A satisfactory and specific treatment of the infected would constitute a significant step in solving the practical problem of human filariasis.

The authors have already published one report on the use of neostibosan as a therapeutic agent in this infection [*this Bulletin* 1943 v 43 54] the present paper constitutes a second report on the progress of the cases therein recorded twelve months after the end of treatment. Data are given in two tables of the 30 native Porto Ricans infected with *Wuchereria bancrofti* and treated with neostibosan, and of the 15 untreated controls similarly infected.

The treated cases received three intravenous injections of neostibosan on alternate days the first being 60 mgm. the second 100 mgm. or 150 mgm. and the third 300 mgm. of the drug. Thereafter 300 mgm. were given daily or on alternate days for 33 or 48 days. The microfilariæ were counted in 60 cmm. of dried and stained nocturnal finger blood at least monthly for 9 to 14 months after treatment.

The authors give the following summary —

"Thirty patients infected with *Wuchereria bancrofti* were treated with neostibosan for from 33 to 48 days. After twelve months 13 of the patients were free of circulating microfilariæ and 5 others had lost from 67 to 99 per cent. of their embryos compared with the number in the blood before treatment. The twelve remaining patients showed little promise of eventual eradication of their infections after observation for nine months.

Of 15 control untreated patients infected with *Wuchereria bancrofti* all remained infected for 14 months of observation. In this interval, 12 showed an over-all increase and 3 showed a decrease in the number of circulating microfilariæ.

Among the treated patients some of whom had been free of microfilariæ for 12 months none presented untoward symptoms referable to treatment.

A. R. D. Adams

MARILL, F. G. & ALCAY, L. Modifications hématologiques chez des noirs sénégalais atteints d'œsophagose entérale (gale filarienne). [Blood Changes in Senegalese Infected with *O. volvulus*] *Bull Soc. Path. Exot.* 1945 v 38 No. 5/6 13-8

TISSAUX J. Troubles de la vue et onchocercose cutanée au Sénégal [Eye Disease and Onchocerciasis in Senegal.] *Bull Soc Path Exot* 1945 v 38 Nos 9/10 311-12.

HUMMELEN L. R. Helminthiasis bij kinderen in het bijzonder binnen het schoolartsdistrict Huizen [Helminthiasis in Children, particularly in the School Medical Officer's District of Huizen.] [Thesis for Doctorate of Medicine University of Amsterdam 30 Nov 1945] 86 pp 1 pl [Numerous refs.] English summary 87-91 1945 Zutphen J B van den Brink & Co

The author examined the faeces of 1 708 schoolchildren in towns and villages of the district of Huizen to the south-east of Amsterdam for worm eggs there were about equal numbers of children of each sex. Ova of *Ascaris lumbricoides* were found in 14.6 per cent of children in 12.2 per cent, and of both species in 4.9 per cent altogether 22 per cent. of the children showed helminth infestation. In different places *Ascaris* infestation varied from 0.9 to 48.7 per cent *Trichuris* from 2.9 to 33.8 per cent, and double infestation from 0 to 17 per cent altogether the percentage varied from 0 to 52.7. Ova of *Taenia* and *Ancylostoma* were not found.

In addition a similar examination was made of 100 schoolchildren of Amsterdam and of 104 of West Terschelling in the former the figures for *Ascaris* and *Trichuris* were 0 and 3 per cent respectively and in the latter they were 35 and 84 per cent respectively.

The degree of infestation depended on the state of local hygiene it was greater in the poorer classes and in rural than in urban communities. It was found that vegetables grown for food were manured with human faeces. Few symptoms were caused and body weight was not affected nor apparently was the intelligence of the children.

The faeces of the same 1 912 children were also examined for ova of *Enterobius* in different localities the rate of infestation varied from 3 to 28.1 per cent average 10.5. A further examination of 1 060 children was made with the glass pestle method of SCHUFFNER and SWELLENGREBEL [this *Bulletin* 1945 v 42 922] and rates of infestation varying from 72 to 100 per cent average 85.2 were found. The high percentage of *Enterobius* infestation is considered to be due to reinfection.

The author considered that the schools did not play a part in the spread of *Ascaris* and *Trichuris* infestation but that they did in the case of *Enterobius* eggs of the last species were found in the dust of a sanatorium.

Fifty five children infested with *Enterobius* were treated with gentian violet—5 mgm. for each year of age three times a day for a week then a week's interval and then the same dosage repeated for another week. The rate of infestation was reduced to about half but after 8 weeks it had again risen to 98 per cent. The author does not recommend mass treatment of schoolchildren with the anthelmintics at present available.

McNAUGHT J B. Laboratory Procedures for the Diagnosis of Trichinosis. *Amer J Clin Path* 1944 Sept. v 14 No 9 Tech. Sect. 87-83 3 figs [18 refs.]

SWELLENGREBEL, N H & SCHUFFNER W A. P. Een methode ter opsporing van besmetting met *Oxyuris vermicularis*. [A Method of Diagnosis of *Enterobius* Infection.] Reprinted from *Nederl Tijdschr v Geneesk* 1943 Aug 21 & 28 v 87 Nos. 34/35 1363-6 3 figs.

See this *Bulletin* 1945 v 42, 922.

BEJLMEK, J. Een uitzonderlijk geval van ocyuriasis van den darmwand. [An Unusual Case of *Enterobius* Infection of the Bowel Wall.] Reprinted from *Nederl Tijdschr v Geneesk* 1944 Jan. 1 & 8, v 89 No. 1/2, 24-8, 10 figs. on 2 pls.

GUILLON, J. Essai de traitement des ocyuriases par la thiodiphénylamine. [The Treatment of *Enterobius* Infections with Phenothiazine.] *Bull. Soc. Path. Exot.* 1945 v 38 Nov 8 10 279-88

PEPPER, O. H. P. & DIAZ RIVERA, R. S. Trichiniasis. A Review of the Clinical Picture and Laboratory Diagnosis of the Disease, with an Analysis of several Cases. *Puerto Rico J. Pub Health & Trop Med.* 1945 Mar., v 20 No. 3 367-76 [Refs. in footnotes.] [Spanish version 377-88.]

In this useful brief survey of trichiniasis the authors bring out well the variety of the possible symptoms and the difficulty which may be encountered in diagnosis. Most of the information given is available in textbooks. After a survey of the American and Spanish literature the authors are impressed by the tremendously high incidence of trichiniasis recorded in some countries of temperate zones in comparison with the tropics where trichiniasis seems to be relatively rare. They are unable to account for this difference, but suggest that it may be due to the greater efficiency of investigation done in the United States and to differences in diet. In the tropics people are so poor that they eat less meat and more carbohydrate and they cook their food more thoroughly (especially those of Spanish descent). Also when diarrhoea and eosinophilia occur together in the tropics they may be ascribed to intestinal parasites without examination for *Trichinella* being made. The apparently low incidence of trichiniasis in the tropics should be investigated further. The authors remark upon the fact that trichiniasis has not yet been recorded from Porto Rico although large quantities of pork products are eaten there and most of these are imported from the United States where DICKMAN (*Bulletin of Hygiene* 1938 v 13 729 found, in Philadelphia, *Trichinella* in 10 per cent. of pork sausage packed at random in the meat markets. The incidence of trichiniasis in the United States determined by post-mortem examinations is 10 to 25 per cent.

The brief description of the clinical picture emphasizes the great variety of " " may be encountered [see also recent abstracts in this *Bulletin*]. The diseases simulated include meningitis polyomyelitis, encephalitis polyneuritis periarthritis nodosa, tetanus (when the masticatory muscles are involved) typhoid fever scarlet fever German measles and erythema multiforme. The authors make the somewhat unorthodox statement that the diaphragm and muscles of the thoracic and abdominal walls are less frequently involved than the gastrocnemii deltoid, biceps and muscles of the eye. For diagnosis they rely upon demonstration of the larvae in the blood, cerebrospinal fluid and muscles and they regard eosinophilia as of great diagnostic value. They demonstrate the larvae in the blood (during the early invasion period) by diluting 5 to 10 cc. of venous blood with 2 per cent. acetic acid and examining the sediment. The cerebrospinal fluid is centrifuged and the deposit examined [cf GAASE, this *Bulletin* 1945 v 42, 481 for the presence of antibodies in the cerebrospinal fluid]. Eosinophilia is not a measure of the severity of trichiniasis because it may be very low in the more acute cases [cf GAASE, this *Bulletin* 1948 v 43 236]. It is a drawback of the precipitin test that it does not become positive until the fourth week. Discussing the limitations of the Bachman intradermal test, the authors say that it sometimes fails in cases of

proved trichiniasis and that in others the reaction is delayed group reactions with other parasites occur and some normal people may give false positives [cf recent abstracts in this *Bulletin*]

The authors record brief details of eight subjects. The first shows the simulation by trichiniasis of an acute abdominal emergency the second its simulation of nephritis and tetanus the third involvement of the eyes and their muscles the fourth the infestation of four youths from the same source (pork) the fifth myocardial damage the sixth extreme myositis the seventh the possible association of trichiniasis with angioneurotic oedema and the eighth its co-existence with asthma.

G Lapage

OLIVER GONZÁLEZ J. Diferencias antigénicas entre la larva y el adulto de la *Trichinella spiralis* [Antigenic Differences between the Larva and Adult of *Trichinella spiralis*] *Puerto Rico J Pub Health & Trop Med* 1945 Mar v 20 No 3 389-418 1 fig [Refs in footnotes]

This is a translation of the author's earlier paper (*J Infect Dis* 1941 v 69 254) (noted by title only in this *Bulletin* 1942, v 39 627). Only the author's main conclusions can be given here some of them have already been mentioned in this *Bulletin* 1944 v 41 225. The author summarizes in the paper under review and in earlier papers [this *Bulletin* 1941 v 38 528] the history of the discovery that when some animals acquire resistance either naturally or by artificial infestation to certain metazoan parasites and, when the living larvae of the parasites concerned (and also the adults of *Trichinella spiralis*) are put into the immune sera thus produced granular precipitates are formed around the external openings of these larvae (mouth anus and sometimes the vulva). The immune sera also have in some instances a parasitocidal action which causes the death and disintegration of the larvae. Precipitates are also deposited in the immune serum.

[BLACKLOCK GORDON and FINE (this *Bulletin* 1930 v 27 880) noted that these precipitates occur in the gut and round the extremities of the larvae of the dipterous insect *Cordylobia antropophaga* which causes myiasis. They have been since observed around the mouth and sometimes also around the anus and vulva of larvae of the nematodes *Nippostrongylus muris* *Ancylostoma caninum* *Trichinella spiralis* *Strongyloides ratti* and *Ascaris lumbricoides* (see Oliver González this *Bulletin* 1944 v 41 223)]

As a result of his studies of this effect of immune sera of rabbits upon the larvae of *Trichinella spiralis* González believes that these precipitates are formed when the secretions and excretions of the larvae or the adults of this species come into contact with antibodies in the immune serum. In this paper he records his conclusion that two types of antibody one antilarval and the other antiadult appear in the serum of rabbits experimentally parasitized by *Trichinella spiralis* and that these have a specific action against the larvae and adults respectively. He suggests that there may be also a third protective antibody inseparable from the antiadult antibody that this nematode may possess at each phase of its development several antigens and that those studied in this paper are only some of those present.

The antiadult antibody causes *in vitro* (in hanging drops) the formation of precipitates around the mouth anus and vulva of the adult *Trichinella*. The oral precipitate is much the most frequent and appears very quickly. The death of the larvae may result (see below). The antiadult antibody can be detected *in vitro* at the end of about 15 days after the infestation its action increases moderately between the 25th and 35th days and begins to decrease until it ceases on the 50th day. It reappears in full activity on the 5th day



after superinfestation, rising abruptly then, reaching its maximum and continuing to increase when infestations are repeated. It then confers on rats a partial immunity against the intestinal phase of the infestation and passive immunity can be transferred from rabbits to rats.

The anti-larval antibody provokes *in vitro* precipitates around the mouth, but not at the anus of the larva. It appears in the serum on about the 30th day after infestation and attains its maximum action between the 45th and 60th days. Its concentration does not increase but remains moderately high during repeated infestations but it gives hardly any passive immunity to rats. The author therefore suggests that it is the anti-adult antibody which is the decisive factor in the transference of passive immunity from one animal to another (e.g. rabbits to rats). For his reasons for this conclusion the paper itself must be consulted.

The anti-adult and anti-larval antigens described in this paper probably constitute the author thinks complete groups of antigens which acting as groups provoke reactions which are qualitatively different, the differences probably depending on the relative proportions in which the various antigens are present and also on the appearance of new antigens as developmental stages succeed one another. The author claims that Table I shows that the anti-adult antibody but not the anti-larval, is active against immature larvae at the moment when they leave the uterus. This suggests the author thinks that immature larvae have an antigenic structure similar to that of the adults. His studies suggest that this antigenic structure begins to develop when the larvae are 20 days old. As the larvae mature new antigenic structures are developed. These antigenic differences may possibly depend upon the fact that the developing embryos and the adults feed upon the intestinal wall, while the mature larvae feed upon red muscle. In other words the antigenicity of the parasite may be related to the enzyme activity of the special tissue which it parasitizes. The differences observed between the different antigens may perhaps be similar to those shown by some lactobacilli which, by fermenting sugars produce changes in their polysaccharide antigens (see MEYER, this Bulletin 1944 v 41 225).

González discusses his results in relation to certain general problems of immunity to helminth infestations. He compares his results with those of CAMPBELL (*J. Immunology* 1938 v 35 465) who found that in rats infested with the larval stages of *Taenia taeniasformis* two types of antibodies appeared, one produced in the first week of the infestation and able to destroy unencysted larval stages of this tapeworm the other produced when the infestation was established and able to destroy encysted larval stages. González also discusses the work of TALIAFERRO (this Bulletin 1940 v 37 887 1941 v 38 110) on the inability of certain antigens to saturate antibodies. González gives the following possible explanations of the failure of some observers to transfer passive immunity to *Trichinella spiralis* or to observe any deleterious action of immune sera *in vitro*: (1) the sera used for transfer of passive immunity were mostly obtained by these observers from animals which had been artificially infested only once and the sera were taken a long time after infestation, or perhaps at the moment when the anti-adult antibody was very scarce in the serum. (2) some observers have used the sera of rats and guinea-pigs which produce González thinks antibodies much less powerful than those produced in rabbit serum. (3) observations on the deleterious action *in vitro* have been made for 24 hours only which is a very short time for their observation. González made observations for as long as 7 days. (4) the movements of the larvae may have dispersed the precipitates in some instances especially when they have not been given sufficient space in the apparatus used. McCoy (this Bulletin 1941 v 38 529) suggested that resistance to *Trichinella spiralis* is

chiefly mechanical the adults being expelled as the result of peristalsis and secretion by the intestinal mucosa of increasing quantities of mucus he doubted the existence of humoral resistance to them. CHANDLER (*Amer J Trop Med* 1939 v 19 309) postulated the existence of a local (intestinal) resistance provoked by antibodies which do not get into the blood in appreciable quantities but are absorbed and retained by certain cells of the intestinal mucosa he thought that this type of resistance may be the most important one in trichiniasis and that the other type of resistance is produced when parasites migrate and liberate antigen into the circulation so that antibodies are produced there TALLAFERRO [this *Bulletin* 1934 v 31 818] believes that the so-called parenteral and intestinal immunity are fundamentally the same and are produced by the same mechanism As TALLAFERRO and SABLES (*J Infect Dis* 1939 v 64 157) have pointed out *Trichinella spiralis* (and *Nippostrongylus muris*) penetrate into the epithelium of the gut and thus impregnate with their secretions and excretions the fluids of the intestinal wall so that infestations with species which do this are in reality parenteral. The existence of an intestinal immunity in the absence or lack of increase of precipitins in the blood demonstrated by BACHMAN and RODRÍGUEZ MOLINA (*Amer J Hyg* 1933 v 18 266) and confirmed by CHANDLER [this *Bulletin* 1940 v 37 216] and by GONZÁLEZ (see the present paper) is due GONZÁLEZ thinks to the fact that the above workers used an antilarval and not an antiadult antigen The view that antibodies do participate in the intestinal phase of the immunity to *Trichinella spiralis* is reinforced by the fact which GONZÁLEZ claims been perfectly proved that the antiadult antibodies increase positively as the infestations are repeated [see also ROTH this *Bulletin* 1944 v 41 59] G Lapage

ROTH H Serodiagnosis of Trichinosis by Microscopical Testing with Living *Trichina* Larvae *Nature* 1945 June 23 758-9 1 fig

Roth (*Acta Path et Microbiol Scandinavica* 1941 v 18 160) described a method of using for the diagnosis of trichiniasis the fact that when living larvae of *Trichinella spiralis* are placed in the serum of animals immunized against this species (immune serum) granular precipitates are formed round the external openings of the larvae and in the serum [see also GONZÁLEZ above and other recent abstracts in this *Bulletin*] This method has since 1941 been used in Denmark and Sweden by Roth and in Norway by HAUGE (*Norsk Vet Tidsskr* 1944 v 56 384) BERGWALL (*Svenska Läkartidn* 1943 v 40 72) and NORUP (*ibid* 1944 v 41 2420) have also reported on it. There have been during recent years several outbreaks of trichiniasis in Norway and Sweden but none in Denmark or Finland.

The test is done as follows Larvae are obtained by artificial digestion of trichinized muscle and washed in sterile saline For each test about 100 sterile larvae are put into the hollow of a sterile thick hollow-ground slide and covered with 0.5 cc. of immune serum which has been centrifuged twice A sterile coverlip excludes all air bubbles The slides are then placed in a moist chamber (made by placing wet blotting paper in a glass dish and covering this with wire netting) and incubated at 37°C They are examined after 5 hours and again after 24 hours [contrast GONZÁLEZ in the abstract above who regards 24 hours as too short a time] If the serum contains antibodies bubble-like or finely granular precipitates are seen mostly around the anterior ends of the larvae After 24 hours the precipitates are chiefly seen in the serum The amount and form of the precipitates vary greatly and depend largely on the age and size of the infestation The reaction usually becomes positive between the 10th and the 20th day after the first appearance of symptoms but in a few instances a faint reaction was obtained before the 10th day The commonest

first symptoms are fever and oedema of the eyelids. From mild cases the antibodies seem to disappear about a year after recovery from the disease. Roth diagnosed 80 subjects in this way and could exclude trichiniasis from the differential diagnosis of 30 others in whom trichiniasis had been suspected. The test was Roth considers more sensitive and more specific than the intradermal or precipitin tests. [The author does not give details of his cases in support of this conclusion.] Similar reliable results "were obtained when the test was applied to pigs (which were positive 17 days after infestation) dogs cats silver foxes and guinea pigs. G. Lapage

STUESSENGUTH Hazel & KLIXE B. S. A Simple Rapid Flocculation Slide Test for Trichinosis in Man and in Swine. *Amer J Clin. Path.* 1944 Sept., v 14 No. 9 471-84 1 fig & 4 charts. [44 refs]

The authors describe a flocculation slide test (also outlined by McNAUGHT below) for the diagnosis of trichiniasis in man and in pigs which can be done in "less than ten minutes" and is they claim simple, sensitive and specific.

The test is a development of Stuessenguth's observation that an alkaline aqueous extract of powdered *Trichinella* larvae has the power of coating cholesterol crystals and of acting as a specific and sensitive antigen in a flocculation slide test. It is suggested that extracts of other injurious agents may act in a similar way and provide antigens for similar flocculation slide tests.

The materials used are essentially the same as those used for the flocculation slide test for the diagnosis of syphilis devised by KLIXE (*J Lab & Clin. Med.*, 1930 v 16 186) see also *Bulletin of Hyg* 1930 v 5 87 1931 v 6 174 & 692]. The antigen used is an alkaline aqueous extract of *Trichinella* larvae. Larvae isolated by digestion from trichinized rat muscle are recovered by the modification of the Baermann apparatus devised for this purpose by HOBWATER and MEYER (*Science* 1937 Dec. 17 568). The larvae are then dried in a vacuum desiccator over sulphuric acid for 24 hours and ground up in a glass mortar to a very fine powder. This powder is then extracted with 4-8 per cent. sodium carbonate solution. From this extract an antigen emulsion is prepared by placing 0.43 cc. of distilled water in a one-ounce bottle and allowing 0.5 cc. of 1 per cent. cholesterol (Pfanztehl C.P. precipitated from alcohol for Klime tests) solution in absolute alcohol to fall drop by drop into the bottle. After rotation of the bottle for 20 seconds on a flat surface, 0.15 cc. of antigen is pipetted into it and the bottle is shaken for 1 minute. Then 1.12 cc. of 0.85 per cent. sodium chloride solution is rapidly run in and the bottle is again shaken for one minute. The emulsion thus obtained is refrigerated overnight and is then ready for use. It retains a satisfactory sensitivity and specificity for 6 weeks if it is kept tightly corked and in the refrigerator. The crystals of cholesterol should then be very small, uniform in size and completely dispersed. If they are not dispersed because the antigen had not coated them another 0.15 cc. of antigen emulsion is added and the bottle is again shaken. Any flaky material found after refrigeration overnight is removed by centrifuging.

The test is done by first heating the serum to be tested to 56°C. for 30 minutes or to 61 to 63°C. for 4 minutes and then pipetting 0.05 cc. of it into the kind of paraffin-ringed slide used for the flocculation slide test for the diagnosis of syphilis. Twelve sera can be tested at one time. One small drop of the antigen emulsion is allowed to fall into the serum from a Wright pipette or from a syringe with a 28-gauge needle. The slide is then rotated on a flat surface for 4 minutes through a circle three-quarters of an inch in diameter at the rate of 150 rotations per minute. Faster rotation reduces the sensitivity of the test. The result is then read at once through a microscope at a magnification of  $\times 100$ . If the reaction is negative the crystals of cholesterol coated with the antigen are completely dispersed and there is no clumping.

In flocculation tests coarse microscopically visible antigen particles require much less antigen to alter their surfaces than is required by those present in the fine dispersions of precipitation (see EAGLE, *Bulletin of Hyg* 1931 v 6 375 KLINE *J Lab & Clin Med* 1931 v 16 1202 and ZINSSER *J Immunology* 1930 v 18 483) In the precipitin test the titre is determined by using dilutions of the antigen solution and an optimal amount of undiluted serum in the flocculation test the titre is determined by using progressive dilution of the serum and an optimal amount of antigen emulsion and it is truly a measure of the antigen content of the serum The use of the paraffin ringed slides and rotation accelerate the reaction

Positive flocculation reactions of the type here described were obtained by the authors with the sera of 14 human subjects. In 13 of these trichiniasis was also diagnosed by clinical evidence biopsy was positive in 9 and negative in one of these 13 and on 3 of them it was not done. One subject not diagnosed clinically gave a positive flocculation test and a negative biopsy the authors suggest that this may have been a false positive

Negative flocculation reactions were shown by 882 human subjects Among these (a) 857 showed no clinical evidence of trichiniasis three of these 857 were infested with *Ascaris Echinococcus* and *Entamoeba histolytica* respectively and 140 gave positive flocculation reactions for syphilis no biopsies were done on these 857 subjects (b) 24 showed some clinical evidence of trichiniasis two of these gave negative biopsies on the remaining 22 biopsy was not done (c) one subject showed clinical evidence of trichiniasis but gave a negative flocculation reaction unspecified parasites had, however been found earlier in the stools of this man and presumably these were *Trichinella* because the authors suggest that the flocculation test on him was a false negative test Study of the sera of three human subjects which gave positive reactions showed that one was positive from the 21st to the 33rd day after infestation the second was positive on the 54th day but became negative 10 months after infestation, while the third was like the sera of pigs tested [see below] positive 10 months after infestation [This persistence of the positive reaction in both human and pig sera and also the fact that the test is apparently specific enough to differentiate between syphilis and trichiniasis and between trichiniasis and infestation with some other intestinal parasites seem to be valuable features]

The value of the test for the diagnosis of trichiniasis in swine was studied by testing the sera of slaughter house hogs and pigs experimentally infested by feeding them with trichinized rat muscle. Negative flocculation tests were given by the sera of 169 pigs. Of these 157 were slaughter house hogs 12 were tested before their experimental infestation these 12 gave negative flocculation reactions for longer than two weeks after infestation. Even the pig which showed the heaviest infestation from which it died in 16 days gave a negative flocculation test up to the day of its death.

Positive flocculation tests were given by the sera of eleven experimentally infested swine. The test first became positive ( $\pm$  to  $+++$ ) in all these at about 2 to 4 weeks after infestation and remained positive for 10 months after The highest titre in swine sera was 1/64 the lowest 1/16 The highest titre in man was 1/128 [the lowest is not stated] The earliest peak of antibody in pig serum was found on the 23rd day and the latest on the 55th day Eleven biopsies were done on the pigs at times varying from 16 days to 7½ months after infestation. Study of the degeneration and necrosis observed around the larvae in the pig muscle suggested that the larvae were maintaining themselves by destroying muscle cells long after they had been encapsulated.

The authors state that in the average case the flocculation reaction does not become positive until about 3 weeks after infestation. The first positive

reaction in both man and swine was obtained between the 14th and 17th days, and the 25th and 27th days. Because the average life of swine fed for the market is about one year and because the reaction may remain positive for 10 months after infestation this simple test is the authors claim a valuable means of testing swine and therefore of preventing human trichiniasis. It involves no disturbance of normal slaughter-house procedures and a number of pig sera can be tested by one man in a few minutes.

The authors give a valuable summary of the literature dealing with serological tests for the diagnoses of trichiniasis. *G Lapage.*

GOULD S. E. A New Type of Trichinoscope. *Amer J Clin. Path.* 1944 Sept. v 14 No 9 Tech. Sect 88-100 2 figs

The author has devised a ring-shaped trichinoscope. The advantages claimed for it are that it is more easily and cheaply made than other types (see, for example McNAUGHT below) and is stronger and gives a uniform compression of muscle.

It consists of two circular glass plates with a diameter of 11.5 cm. and a thickness of 3.3 mm. with ground edges. The top surface of the bottom plate may be ruled with parallel lines at intervals of 1 mm. These glass plates are held in flat metal rings which have an outer diameter of 13.4 cm. and an inner diameter of 10.8 cm. The outer 8 mm. of the width of each metal ring is 4 mm. thick the inner 5 mm. of the width of both of them is however counterbored to a thickness of 2 mm. The glass plates are thus held in position in a shallower (counterbored) space between the two rings. The metal rings may be chromium-plated. Compression of muscle placed between the glass plates is applied by means of two winged screws set at opposite sides of the rings which screw down upon bolts fixed to the lower metal ring. Photographs of the trichinoscope show both its separate parts and the assembled instrument.

*G Lapage*

McNAUGHT, J. B. Laboratory Procedures for the Diagnosis of Trichinosis. *Amer J Clin Path.* 1944 Sept. v 14 No 9 Tech. Sect 87-88 3 figs. [18 refs.]

## DEFICIENCY DISEASES.

PLATT B. S. Tables of Representative Values of Foods commonly used in Tropical Countries. *Med Res Council Spec Rep Ser* No 253 41 pp. [Numerous refs.] 1945 London H.M. Stationery Office. [8d.]  
Summary appears also in *Bulletin of Hygiene*]

Tables of the nutritive value of foods are a basic need in any surveys of nutrition, and there is wide demand for such a publication as this for use in tropical countries. The values given here are obtained partly from an extensive survey of the literature and partly from analyses of samples collected by the Nyasaland Nutrition Survey. An attempt has been made to assess the weight to be attached to the various analyses and to arrive at representative values for a suitable range of foodstuffs. These values are considered to be sufficiently well founded for the purpose for which they have been compiled, namely the evaluation of dietary data based on records of group intake. They are not suitable for surveys by the individual method, nor for precise nutritional investigations in individual human and animal subjects.

Figures are given for 233 foodstuffs representative of the dietary commonly found in tropical countries. Values given refer to the portion usually eaten, and, where possible a figure for wastage is shown as a percentage of the food as purchased. The water content is given as accurately as possible but the

nutrient values shown may have to be adjusted to a value for water determined individually. Several more or less alternative common names are given as well as the botanical names but it seems likely that investigators may find difficulty at times in placing certain local foods.

H E Harding

EDISON Ann O SILBER R. H & TENNENT D W The Effect of varied Thiamine Intake on the Growth of Rats in Tropical Environment. *Amer J Physiol* 1945 Oct 1 v 144 No 5 643-51 3 figs [14 refs]

Comparable groups of rats were maintained under two environmental conditions a tropical environment of 90°F and 70 per cent humidity and a temperate one of 72°F and 50 per cent humidity. They were given a basal diet of casein dextrose hydrogenated vegetable oil salt mixture and cod liver oil. Vitamins of the B group were either added to the diet or given separately in constant adequate amounts except for thiamin the quantity of which was varied from 300 to 2μ gm daily. When placed in a tropical environment rats lost weight rapidly but after a few days resumed growth at a stable but slower rate. Food consumption in tropical conditions decreased by 30-50 per cent. the anorexia was not due to thiamin deficiency. The weight of these rats was 15-25 per cent less than that of rats given a similar diet *ad libitum* in temperate conditions but 15-25 per cent greater than that of animals in the temperate environment whose diet was restricted to amounts exactly similar to those taken by the tropical animals.

When the thiamin intake of rats kept in each environment and previously given adequate amounts of thiamin was reduced to 2μ gm thiamin daily, the rate of loss of weight was less under tropical than under temperate conditions. There were indications also that polyneuritis developed more rapidly under temperate conditions.

Assays of the livers of these animals showed that the thiamin content varied with the dietary intake but was unaffected by changes of environment. The authors conclude that the thiamin requirements for the growth of rats in a tropical environment are not greater and may be less than in temperate conditions.

H E Harding

BIEN W N Bisulphite Binding Substances in Human Blood. *Chinese Med J* Washington 1944 Oct-Dec. v 62 No 4 358-65 [15 refs]

The blood content of bisulphite binding substances was determined in various clinical conditions. The results are not conclusive enough to warrant the assumption that whenever the B.B.S. are elevated, beriberi is present. The present experience indicates that only when renal insufficiency starvation and diabetic acidosis are not present an elevation of the B.B.S. in the blood may indicate beriberi. Conversely a lack of increase of B.B.S. in the blood does not rule out beriberi. The possible substances in the blood which combine with bisulphites are enumerated and briefly discussed.

TROWELL H C. & MUWAZI E. M. K. A Contribution to the Study of Malnutrition in Central Africa. A Syndrome of Malignant Malnutrition. *Trans Roy Soc Trop Med & Hyg* 1945 Dec. v 39 No 3 229-43 4 figs on 3 pls [38 refs]

This paper appears to have been written earlier than one published by the same authors in *Arch Dis Childhood* (this *Bulletin* 1946 v 43 143). It describes some features of a syndrome common in Uganda as observed in 200 patients at Kampala in 1943. The condition accounted for about 10 per cent

of the medical admissions of adults and about 50 per cent. of the children. Of the 144 adult cases 25 were fatal, as were 10 of the cases in children.

Rough estimates are given of the diets of the natives amongst whom the condition occurs commonly. These show that the very poor labourer's diet is seriously deficient in everything except ascorbic acid; the immigrant labourer's diet is seriously deficient in calories, protein, calcium, vitamin A and nicotinic acid, and moderately deficient in iron and thiamin; the Ganda peasant diet on to which most of the children concerned were weaned when well into their second year is moderately deficient in protein, calcium and nicotinic acid, and probably somewhat deficient in vitamin A, thiamin and riboflavin.

The soft brown hair and pallor of the facial skin that are a common early sign in children are often absent in adult cases. Children seldom show the crazy-pavement dermatosis of adults and many of them have no looseness of the bowels. Most of the features of the syndrome however are present at all ages. The clinical picture consists of a gross loss of body weight in adults or a failure to grow in children; oedema, pallor of the skin and hair; crazy-pavement dermatosis; loose stools; steatorrhoea in children; macrocytic anaemia, slight mental and neurological changes and a deficiency radiographic bowel pattern.

In the absence of sufficient details of the radiographic appearance of the normal African small intestine the authors accept only segmentation, gross irregularity, coarseness or loss of the mucosal folds as evidence of abnormality. Of 23 adults examined, 19 showed frank segmentation, five had an abnormal mucosal pattern and none was normal. 7 of the 9 children examined showed frank segmentation.

Undigested remnants of food were found in the faeces of about half the cases.

Mean figures and the range are given for blood counts on the 200 cases. The syndrome was usually accompanied by a macrocytic hypochromic anaemia, but at times the anaemia was normocytic and not infrequently orthochromic. Examination of the sternal marrow in 101 cases showed a normoblastic erythropoiesis. Plasma proteins are given for 11 adults and 3 children. The mean plasma albumin was 2.05 gm. per 100 ml. with a range of 1.10 to 3.02; the mean plasma globulin was 4.05 ranging from 1.44 to 8.77. The albumin/globulin ratio was less than 1 in all but 2 cases.

Details are given of autopsies on two male adults.

On the ordinary hospital diet progress was slow in every respect. When thiamin was given in addition to the basic diet, definite improvement was reported by many of the patients usually within 5 days. The improvement was largely subjective; no change was noted in the oedema. Giving nicotinic acid to patients taking the basic diet also led to an improvement in the condition of the majority usually within a week. This consisted of a peeling of the dermatosis; no definite effect on the diarrhoea was observed. Injections of crude liver extract led to a reticulocytosis and a satisfactory increase of red cells and haemoglobin in almost all cases.

The syndrome appears to be distinct from pellagra and from nutritional oedema; it is very resistant to treatment by improvement of the diet or by supplements of the common vitamins, and it has a high mortality. It is proposed to call it "malignant malnutrition." H. E. Harding

GILLMAN J. & GILLMAN T. Structure of the Liver in Pellagra. *Arch. Pathology* 1945 Oct., v. 40 No. 4 239-63 22 figs. [Refs. in footnotes.]

This long but interesting paper gives first a detailed account of the histology of sections of livers obtained by biopsy from 120 pellagrins on the day of their

admission to hospital. The livers are divided into four groups, each with further subdivisions that depend upon the quantity of fat present. In the first group the livers show varying amounts of fat only. Livers in the second group show cytosiderin (haemosiderin) and cytolipochrome (haemofuscin) in discrete granules in hepatic and Kupffer cells. The third group is similar to the second but iron-containing pigment is found also aggregated in large masses in cells lying either in the hepatic lobule or in portal tracts. The last group shows pigment cirrhosis. Fatty livers of the first group are the invariable finding in infants suffering from pellagra. No disturbance of iron metabolism is found at this age. Pigmented livers with or without visible fat are found in adolescents and adults.

Evidence is given that pigment is formed in the cells at a time which coincides with the disappearance of fat. The amount of pigment formed varies from case to case, the extent and the intensity of pigmentation giving an excellent indication of the degree of chronicity of the disease. The iron pigment arises within the liver cells as a result of a profound disturbance of intracellular metabolism induced by dietary imbalance. Both pigments appear to originate from mitochondria. Exacerbations of the acute stage may lead to reappearance of fat in livers which already show pigmentation from previous damage.

Repeated attacks of pellagra may cause a fatty condition to progress to frank pigmentary cirrhosis. Such cirrhosis was found in an eighth of all the pellagrins examined or in 15 per cent. of the adults. There was strong presumptive evidence that the incidence of cirrhosis might be as much as 30 per cent. Pigment cirrhosis occurred mainly under the age of 40 years and was indistinguishable clinically and pathologically from haemochromatosis. Evidence is given for the view that this condition is not a result of an inborn error of metabolism but is one of the manifestations of chronic malnutrition.

The authors believe that therapy and the assessment of its effectiveness in pellagra should be based not only on the clinical picture but more especially on the structural alteration in the liver in each case. They suggest that in pellagrins fatty change, formation of intracellular pigment with or without cirrhosis and hepatic carcinoma represent different patterns of reactivity of liver cells to acute and chronic malnutrition.

*H. E. Harding*

GILLMAN J. GILLMAN T. & BRENNER S. Vitamin A and Porphyrin-like Fluorescences in the Livers of Pellagrins, with special reference to the Effects of a High Carbohydrate Diet and Methionine. *South African J. Med. Sci.* 1945 Sept. v. 10 No. 3 67-88 4 figs. [36 refs.]

Fragments of liver obtained by biopsy from 60 adult and infant pellagrins were examined by fluorescence microscopy for the presence of vitamin A. There appeared to be a reciprocal relationship between the amount of fat in the liver cells and the amount of vitamin A fluorescence in the Kupffer cells: there was very little fluorescence in very fatty livers. In rather more than half the cases examined the amount of fluorescence was well below the average normal. The effects of a diet free from vitamin A but containing a high proportion of carbohydrate were erratic: the amounts of vitamin A fluorescence varied in an unpredictable manner. Administration of large quantities of vitamin A in conjunction with a full diet appeared to aggravate the disease and did not lead to as great an increase in vitamin A fluorescence as did ventriculin with a similar full diet. The fatty livers of two pellagrins did not respond to methionine and there was afterwards a delay in the response to ventriculin.



Phrynoderma was observed in two patients whose livers showed marked vitamin A fluorescence three patients whose livers showed no fluorescence had no evidence of phrynoderma. It is concluded that phrynoderma cannot be regarded as due to vitamin A deficiency.

A porphyrin like fluorescence was seen in the liver cells of a few pellagrins [More details of this are given in the following paper] *H E Harding*

GILLMAN J GILLMAN T & BREWSTER S Porphyrin Fluorescence in the Livers of Pellagrins in relation to Ultra Violet Light. [Correspondence.] *Nature* 1945 Dec 8 689.

The examination, by ultra violet fluorescence microscopy of frozen sections of fragments of livers removed by biopsy from 20 African pellagrins soon after admission to hospital, showed the presence of an intense scarlet-red fluorescence in eight cases. Reasons are given for believing that this fluorescence was due to a porphyrin. Patients kept on a carbohydrate diet poor in vitamins lost this fluorescence in their livers exposure of the patients to ultra-violet light then led to a recrudescence of the fluorescence but not to aggravation of the skin lesions. Traces of porphyrins were found in the urine of only one patient.

The authors conclude that (1) Porphyrin fluorescence in the liver can occur during the acute phases of pellagra. (2) The great accumulation of iron pigment in many livers of adult African pellagrins is probably caused by the disruption of an intracellular iron porphyrin complex, such as catalase and cytochrome present normally in the liver cell. (3) Treatment with vitamin B complex is not required to resolve the porphyrin fluorescence in the livers of pellagrins while on a carbohydrate vitamin-poor diet. (4) Ultra-violet light can excite a recrudescence of the porphyrin fluorescence in the liver without causing an exacerbation of the other external manifestations of the disease. Massive quantities of porphyrins can appear in the liver cells without any detectable amounts in the urine. (5) These experiments emphasize the close inter-relationship between the reactivity of the skin to ultra violet light and the deposition of iron and the appearance of porphyrin fluorescence in the liver of African pellagrins. *H E Harding*

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### SPRUE.

LEISHMAN A. W. D. Thoughts on Sprue after Experience in India. *Lancet* 1945 Dec. 22, 813-15 [17 refs.]

From 1942 to 1945 the incidence of sprue amongst troops in India and the South-East Asia Command has been particularly heavy in 1944 alone 675 patients were invalided on account of this disease. The diagnosis of this syndrome presented few difficulties when it was recognized that dysentery alone was not the sole cause of diarrhoea in the tropics. On the therapeutic side there remains considerable need for improvement and even the most specific remedy liver extract acts in a manner quite unknown. Though in India there appears to be reluctance in recognizing sprue in Indians nevertheless this attitude does not appear to be wholly justifiable. What has been termed the malaric syndrome when coincident factors of malaria dysentery ankylostomiasis and malnutrition have been eliminated appears to be indistinguishable from sprue. A somewhat novel observation is that three-quarters of the [European] patients had less than 2 years tropical service when they first developed the disease that length of residence is scarcely a factor as has been previously assumed, was illustrated in one patient, who disembarked

from his ship in Bombay with fully-developed sprue after having spent 2-3 weeks in Durban on his way from Britain. In war time sprue observed a distinct seasonal incidence from March to September with a peak incidence in June during the months corresponding to the fly season (with consequent dysentery) and to the malaria transmission season.

Sixty five per cent. of cases originated in Bengal Assam and Burma but 15 per cent. came from Western India, 13 per cent. from South India and Ceylon and 5 per cent from North India one-third were soldiers living on full rations and usually in an entirely innocuous climate.

In view of the work of HOWAT which indicated that the use of sulphaguanidine in bacillary dysentery provokes steatorrhoea it is striking that a history of frank dysentery was obtained in only 9 per cent. of cases of these 4 per cent. were amoebic 3.5 per cent. bacillary and the rest clinical.

In more than half of the patients the syndrome was fully established within two months of the onset of diarrhoea but in 20 per cent. the interval was as short as 3 weeks. Loss of weight was an outstanding feature and in 95 per cent it was not less than 20 lb. Almost all the patients had changes affecting the mouth lips or tongue 20 per cent had skin changes—follicular hyperkeratosis (a sign of vitamin A deficiency) and parakeratosis (probably a vitamin B deficiency). Well marked pigmentation especially of the face was occasionally seen but never the skin changes of pellagra.

Dark-adaptation tests and slit-lamp examinations of the cornea showed no significant abnormalities in patients so tested.

*Dyspepsia.*—Flatulent dyspepsia was invariably present increasing towards the latter part of the day a common symptom was retrosternal burning pain.

*Stools.*—One important fact emerges. In 20 per cent. of cases there was no apparent increase of fat in the stools. A possible explanation is that owing to the increased bulk of the faeces due to debris and bacteria, a sample estimation does not give a true picture of fat excretion. A second anomaly concerned the pigment in the stools the presence or absence of which affords no real indication of the fat content for stools of normal colour have been found to contain great excess of fat, and *vice versa*.

Leishman reverts to a formerly widely held hypothesis that the normal stool pigment in sprue is reduced to a colourless compound and that this constitutes a classical feature of the syndrome. [A reduction product of hydrobilirubin in sprue was described by NENCI and an account of its chemistry is given by VAN DER SCHEER in *Mense's Handb der Tropenk* 1905 v. 1 20. This was investigated by the reviewer in Ceylon. A colourless extract was obtained by trituration of the freshly passed faeces in 90 per cent. alcohol and filtration. When exposed to the sunlight or shaken with air the extract changed to light yellow or brown. The same effect was produced by the addition of a drop of nitric acid. There appeared to be grounds for supposing that hydrobilirubin is present in sprue faeces but that the greater part is reduced to leucourobilin. That normally coloured bile is secreted in sprue has been ascertained at post-mortem. According to STRASBURGER, *Die Fäzes des Menschen* 1910 leucourobilin is identical with urobilinogen. See also a Report on Researches in Sprue in Ceylon 1912-1914 Cambridge University Press pp 50-51.]

More than half the cases had acid curves (by test meal) within normal limits.

The author satisfied himself that full recovery from sprue could be made in India and he supports the opinion that when once a patient has fully recovered a return to India may be permitted. There were seven fatal cases a case-mortality rate of about 1 per cent. The cases which give rise to anxiety are those which are profoundly emaciated with a striking degree of hypotension,

although there is some dehydration, hydration achieves only limited improvement and desoxycorticosterone is without effect. In cases of this type there is consistently a diminished plasma volume with low blood sodium and chloride the potassium level being normal. Plasma proteins were slightly diminished but not to the extent found in starvation cases. In the few cases in which hypochloraemia, as well as the dehydration was treated, the response was not striking plasma transfusion had little advantage over saline. It seemed clear that no form of parenteral therapy could act as a substitute for food given by the mouth.

As regards aetiology the author considers that in many respects sprue behaves like an infection although usually sporadic it occasionally attains epidemic proportions. In 1943 in Chittagong nine separate units were affected and in some the incidence was 50 per cent. In one R.A.F. unit within 3 weeks of arrival there 10 per cent of the men had diarrhoea which rapidly developed into sprue. It was thought at the time that some tinned meat might have been a factor in causing the initial enteritis. The popular idea of "sprue houses" would suggest some infective agent but none has yet been found.

The author agrees with SROEVERS (1942) that interference with the absorptive process is the result of failure in the phosphorylation of fatty acids. The primary failure in sprue is lack of vitamins of the B group (well-known and [perhaps unknown] for without these phosphorylating enzymes cannot be constituted. By accepting this view however difficulties are encountered, for in sprue a history of inadequate vitamin-intake is seldom obtained. The recent knowledge of biosyntheses by intestinal bacteria. BENZESON [*Bulletin of Hygiene* 1945 v 20 564] provided evidence that nicotinic acid is synthesized by aerobic and destroyed by anaerobic organisms within the human intestine and that in health an equilibrium must exist between those which produce and those that destroy vitamins. The infective character of sprue may now become capable of a more liberal interpretation, and be linked with the conception of sprue as a deficiency disease synthesizing organisms may be swamped by infection with non-synthesizing organisms which otherwise are not pathogenic and stagnation in the small intestine due to unaccustomed diet may provide a medium in which the latter flourish.

This hypothesis has the merit that it can be put to the test. A series of vitamin-excretion estimations in patients with sprue and in controls on a standard low vitamin diet should be made together with an investigation of the small intestine flora on the lines employed by BENZESON to determine the relative proportions of aerobes and anaerobes and their ability to synthesize nicotinic acid and other members of the B group. For this purpose samples must be collected by means of the Miller Abbott tube which, it has been found, can be used in sprue.

Philip Manson-Baker

KEELE, K. D. & BOUND, J. P. Sprue in India. A Clinical Survey of 600 Cases. *Brit Med J* 1946 Jan. 19 77-81 2 figs.

For the present purpose sprue is defined as a syndrome consisting of diarrhoea, with the passage of light-coloured stools of high fat content, sore tongue flatulent dyspepsia and emaciation. Malnutrition may indeed manifest itself as the sprue syndrome, but steatorrhoea is too variable a feature upon which to separate the two and the syndrome as defined above has been diagnosed as sprue "even in the presence of an isolated normal faecal fat."

Throughout India during the recent war period the incidence of sprue was highest in May and June it was minimal in November December and January in both 1943 and 1944. This applied whether the cases originated in the cool climate of the Assam Hills (54 per cent.) or in the hot plains of Bengal

and Bihar (23 per cent) or in the rest of India (23 per cent.) The geographical distribution of 450 cases was Assam and N Burma 54.2 per cent. Bengal and Bihar 23.1 per cent. S India and Ceylon 9.1 per cent. Bombay Presidency 8.9 per cent. NW and Central India 4.7 per cent. Within a climatic zone sprue is regional. For instance 14 per cent. of cases in the present series occurred near Imphal and the high incidence in this place continued long after the siege had been raised. Chittagong (9 per cent) on the coast at the edge of the Ganges delta produced quite a nest of cases—six from one aerodrome in two weeks. The difference in climate between these two localities illustrates how the local regional factor may supersede that of climate. The maximal incidence occurred after one or two years service in India. The earliest was in the Red Sea *en route* to India. Heat adaptation was probably not an important factor.

In a comparison of the seasonal incidence of sprue and dysentery (amoebic and bacillary) it was found that the incidence of sprue commonly precedes that of dysentery suggesting that it is unlikely that sprue commonly follows an attack of dysentery. In 23.6 per cent of cases dysentery preceded sprue but there was no significant difference between the incidence of dysentery in the cases of sprue. In some individual cases however a close relationship is found to exist between an attack of amoebic or bacillary dysentery and the sudden passage of sprue stools the effect of the dysentery may be non specific in activating the latent syndrome. In one group of 87 cases labelled malnutrition in the Chindit Forces (in June and July 1944) were included 52 with the sprue syndrome. Analysis of the stools of 15 showed 12 with faecal fat over 30 per cent. Malaria was frequent and whilst response to sprue therapy was unsatisfactory improvement was dramatic after the development and subsequent treatment of malaria. Although the brunt of incidence of sprue falls on Anglo-Indians and Europeans it is undoubtedly true that Indian troops have developed the full syndrome during this war.

Regarding the influence of diet little information of value was forthcoming. Most of the patients developed diarrhoea under jungle conditions but many were on field service rations. A large number became ill on a diet composed of protein 95-103 gm fat 114-143 gm carbohydrate 425-435 gm with calcium 1.6-1.7 gm iron 20-25 mgm. vitamin A 1450 I U thiamin 1.2-1.8 mgm riboflavin 2.1 mgm niacin 16.3 mgm ascorbic acid 6 mgm (with supplementary tablets of 50 mgm). This diet well balanced and adequate as it appeared, was found monotonous and distasteful.

In contrast to the classical picture the type of medical history was as follows.—After jungle training and contracting the customary short fevers and dysentery the soldier became involved in fighting in Burma and subsisted on the diet already detailed. The onset of diarrhoea was gradual and was usually attributed by the patient to his diet. Soon anorexia and glossitis were noted with flatulent dyspepsia and heartburn. After reporting sick he was admitted to hospital and rapidly improved but on returning to duty the diarrhoea recommenced and the typical sprue syndrome evolved. The result might be mild acute sprue with continual relapses if as so often happened he was returned to duty in India. The severe form proceeds from the onset to produce dehydration emaciation and a smooth dry tongue. Steatorrhoea is obvious. Severe anaemia may develop suddenly necessitating transfusion. Though response to treatment is often satisfactory men with this type had to be evacuated from India. On an average the period between onset and evacuation was about one year in both mild and severe cases.

Post-dysenteric sprue was noted especially after amoebic dysentery in these cases the sprue syndrome was either temporary or severe and long

Several instances of subacute hepatic necrosis without jaundice were observed in which there were symptoms of sprue—the latter improved as the liver diminished in size.

The clinical picture of incomplete sprue was seen in 3.6 per cent. of cases—the diagnosis noted on the finding of steatorrhoea and other signs of sprue in cases of chronic diarrhoea which had been treated as chronic dysentery. At the other extreme are cases of glossitis with minimal steatorrhoea conveniently termed "larval sprue." In this series 20 per cent. had total faecal fat of less than 30 per cent. and it is more than probable that the numbers with normal fat excretion would have been greatly reduced had it been possible to repeat the examination.

Glossitis was practically constant (96 per cent.) in this series and the longer the cases were observed the fewer were the exceptions. The tongue changes were found very variable but coincided within a day or two with diarrhoea. Glossitis responded surprisingly quickly to diet, but administration of nicotinic acid and riboflavin often seemed to accelerate improvement. Cheilitis and angular stomatitis occurred in 40 per cent. and did not respond so quickly. The typical magenta tongue of riboflavin deficiency was not seen. The appetite ranged from extreme voracity to extreme anorexia. Rash increase of diet, on the return of appetite provoked relapse. Vomiting was present in 18 per cent. particularly in cases of acute onset. Heartburn was common, and caused considerable distress—dysphagia was not marked. Dyspepsia, on the other hand, of the flatulent type was practically constant (94 per cent.) and was exacerbated by administration of fats—the gastric juice, however was normal in at least 68 per cent. Distension, a salient feature appeared early and disappeared late, being maximal in the hypogastrium. The abdominal girth altered by 1-2 in. only though the patient's sensation leads him to expect more. Barium meal examinations failed to show convincing evidence of small intestine dilatation, but one instance of megacolon was found in one who did not exhibit undue distension but made a good recovery. Diarrhoea often as acute and as painful as in dysentery with passage of 15-20 pale watery stools was a constant feature and its response to sulphaguanidine was similar to that of dysentery but the stools were devoid of exudate and there was neither pyrexia nor leucocytosis. The onset of sprue was often sudden and unexpected. Diarrhoea preceded glossitis by about six weeks in 80 per cent. of the cases—the reverse very rarely.

On admission most patients had lost 25 per cent. of their normal Indian war time body weight. The average loss ranged from 20 to 60 lb. at body weights of 130 to 195 lb.

Cramps usually in calves and thighs, were present in 25 per cent. No osteoporosis was observed. Chvostek's and Trousseau's signs were negative except in one solitary case. Response to liver nicotinic acid, calcium gluconate, salines and transfusions was satisfactory from the clinical viewpoint.

Dry skin with depilation was common, whilst scaling of parakeratotic type occurred in 27 per cent. Follicular hyperkeratosis responded quickly to treatment and cleanliness and, though it suggested a vitamin A deficiency dark adaptation tests were normal in 19 of 20 patients with one exception. Pigmentation occurred in 4 per cent. and was so extensive in one patient as to suggest haemochromatosis. The distribution did not suggest pellagra.

Hypotension below 100/70 was noted only in 8 per cent. all severe cases with dehydration and low urinary chlorides—this hypotension persists and rises slowly in response to treatment. No evidence of left or right-sided heart failure was found.

It was thought that these cases would present examples of typical deficiency states but this did not turn out to be so. In some obdurate cases of glossitis

nicotinic acid proved effective but though glossitis with angular stomatitis was common other signs of riboflavin deficiency were absent. No case showing evidence of vitamin B<sub>1</sub> or C deficiency was seen.

Pallor of the faeces at some period was almost constant and was due not only to the high fat content, but also to alteration of bile pigment. A pale stool may have a normal fat content a coloured stool may have a raised fat content. Microscopically fatty acid crystals fat globules and soaps may be seen but give little guide to quantitative fat excretion. Analysis of single stools showed great variability two consecutive specimens for instance showed 21 per cent. and 36 per cent. total fat content respectively. For routine examination 24-hour collection of stools well mixed, should be a minimum procedure. A further proviso is that the daily fat intake for at least the three previous days should be known. In 10 normal persons the total fat averaged 30 per cent. on a fat intake of 70 gm daily but in 20 per cent. of the cases of sprue the faecal fat was below 30 per cent. conversely high faecal fat above 50 per cent. did not indicate clinical severity. Fat splitting was excessive in the majority of 274 cases the ratio of split to unsplit fat was between 3-1 and 10-1. The high ratio might be interpreted as due either to delayed absorption or to excessive lipase action. Hyperchlorhydria or normal acid curves were present in 68 per cent. in 27 per cent. hypochlorhydria (less than 10 units HCl) was present.

Severe anaemia was uncommon even in clinically severe cases though blood crises were observed in a few. The few blood-sugar curves which were carried out showed normal fasting values with the low rise as generally described in sprue.

The object of treatment was to make the patients fit to travel and the authors have not made innovations they do however remark on the value of parenteral crude liver extract in severe cases. The response to sulphaguanidine in acute cases up to a total of 70 gm. was found to be good. Immediate prognosis for life was good. No patient in the 600 of this series died. Of 40 cases followed up for one year six have had severe relapses and the remainder less severe recurrence of symptoms none has remained quite well.

Philip Manson Bahir

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## HAEMATOLOGY

EVANS R. W. Anaemia associated with the Sickle Cell Trait in British West African Natives. *Trans. Roy Soc Trop Med & Hyg* 1945 Dec. v 39 No 3 207-20 [12 refs.]

A diagnosis of sickle cell anaemia based solely on the association of anaemia with sicklaemia is unjustified, as factors other than sickling of the cells may be responsible for the anaemia of patients with the sickle cell trait. In one series of patients suffering from anaemia associated with sicklaemia the sickle cell haemolytic crises may well have been initiated by anaemias of different aetiology. Complete haematological investigations showed such underlying conditions as megaloblastic nutritional anaemia hypoplastic anaemia of undetermined origin and anaemia due to hookworm infection dietary deficiency and malaria. In unmasking the bases of these anaemias the value of bone marrow examinations has been shown repeatedly. During a sickle cell crisis the marrow shows an intense erythroblastic and leucoblastic hyperplasia with considerable increase in the number of monocytes many of which may contain engulfed red cells. The normoblasts tend to be large early eosinophilic forms

with a well patterned nucleus such as are found in haemolytic anaemias and in conditions of prolonged loss of peripheral blood. The diagnosis of a sickle cell haemolytic crisis will therefore be suggested by an anaemia with leucocytosis jaundice and a hyperplastic bone marrow which shows no abnormal cells occurring in a patient whose red cells have been shown to exhibit sickling *in vitro*. It is then confirmed by the demonstration of sickle cells *in vivo*.

In a second series of patients the sickle cell crises appeared to have been precipitated by other more urgent diseases or acute toxic conditions such as tropical myositis and blackwater fever meningitis and Addison's suprarenal disease. In these the spleen at autopsy presented as a small hard, nodular grey organ. Cut sections showed thickened trabeculae and yellowish-brown nodules scattered throughout the pulp—the result of organization of haemorrhagic areas. The pulp itself had been transformed into a reticular mass packed with sickle cells. These extensive degenerative changes may be taken as evidence of frequent sickle cell crises that had occurred in the past. Lesions found in other organs are fundamentally similar to those which have been described in the spleen namely tissue destruction by haemorrhage and thrombosis followed by necrosis. These observations suggest that the chief feature of the condition is not the anaemia but the liability to thrombosis which occurs during a sickle cell crisis. The term "sickle cell disease" would therefore appear to be preferable to "sickle cell anaemia". *F. Margatroyd.*

ALTMAN A. The Sickle-Cell Trait in the South African Bantu. *South African Med J* 1945 Dec. 8 v 19 No 23 457 20 refs.]

"Of 403 blood specimens of South African Bantus only one showed the sickle-cell trait in a moist sealed preparation after 24 hours incubation at 37°C. The sickle-cell trait which is very common in the West African and American negro is rare in the South African Bantu."

WOOSTER A. C. DICK, W. S. & BIERING W. L. Sickle Cell Anemia in White Patients with Ulcers of the Ankles. Report of Two Cases. *Arch. Intern. Med.* 1945 Oct. v 76 No 4 230-33 4 figs. [Refs. in footnotes.]

Sickle cell anaemia is almost exclusively a disease of the Negro race, although several instances of the disease have been reported in patients thought to be without Negro ancestors. Ulcers on the legs or ankles unilateral or bilateral, have appeared spontaneously or after mild trauma in Negro patients suffering from this condition healing is prolonged and followed by scarring. Hitherto however all available case histories of the disease in the white race have failed to mention or have noted the absence of ulcerations or scars about the ankle joints.

The present report describes two patients from one family suffering from sickle cell anaemia, with ulcers of the ankles and limitation of motion about the ankle joints. The first patient a 20-year-old white youth was admitted to hospital complaining of ulcers on both ankles the ulcers having appeared when he was 13 years of age after an attack of dermatitis venenata (ivy poisoning) and having persisted until the time of his admission to hospital. The second patient the 14-year-old sister of the first, had a small ulcer on the right ankle which had existed for approximately three weeks. Both patients were anaemic and 15 and 18 per cent respectively of their erythrocytes showed sickling. Other physical and laboratory findings were confirmatory of sickle cell anaemia the Wassermann and Kahn reactions were negative. The family history revealed that the paternal grandmother had been pale and suffered from ulcers of the ankles, and that the father and an uncle had both been pale and had had scarring and fixation of both ankle joints. The parents

of the grandmother the first reported member of the family with the disease were known by a local historian to have been normal and of the white race. [The remainder of the ancestry is not recorded it may have contained a negroid element.]

F Murgatroyd

TOMLINSON W J A Study of the Circulation of the Spleen in Sicklaemia and Sickle Cell Anemia. *Amer J Path* 1945 Sept v 21 No 5 877-87  
6 figs on 8 pls [12 refs]

Histological changes in the spleen in sicklaemia have been stated to be congenital in origin but in a large number of cases no congenital vascular abnormalities have been found. It is possible therefore that the splenic picture may result from the sickle cells.

In the normal spleen follicular capillaries arise from the central arteries pass through the substance of the follicles and terminate just beyond the marginal zone by numerous small openings into the red pulp always at considerable distances from the nearest venous sinuses. Follicular capillaries frequently unite by short branches. In some instances the endings are distended presenting ampullae with restriction of erythrocytes but permitting the escape of plasma through the endothelial walls. In others large openings between the endothelial cells allow the passage of erythrocytes into the pulp cords and thence through stomata into the venous sinuses. Capillaries of the marginal zone arise from branches of the follicular capillaries passing into the red pulp where they branch the small branches terminating in the marginal zone of the follicle in the pulp spaces. The tips of these capillaries are usually distended into thin walled ampullae with narrow clefts leading into the pulp spaces. Capillaries of the pulp cords are branches of the capillaries of the marginal zone and terminate in the pulp spaces with or without ampullae and in some cases perhaps open directly into the venous sinuses. It seems however that the circulation of blood in the spleen is open with the pulp spaces constituting the connexions between the arterial and venous channels.

Routine autopsy sections of spleen from 150 cases of sicklaemia and 24 cases of sickle cell anaemia showed no evidence of congenital or other abnormalities of the arteries or arterial capillaries. In most cases pooling in the marginal zone was marked. The sickled erythrocytes were compressed and packed, usually in a circular lamellated fashion with obvious overlapping in the dilated pulp spaces. The venous sinuses were generally collapsed.

In preparations perfused through the arteries the erythrocytes were washed out of the arteries arterial capillaries and the venous sinuses but were present in the pulp cords especially in the marginal zones which obviously represented the pools. There was no evidence of abnormal dilatation congenital defects or of direct emptying into the venous sinuses. It is impossible therefore to explain the pooling in the marginal zones by changes in these arterial capillaries.

Venous perfusion produced filling of the small venous sinuses with erythrocytes and emptying of the arterial channels. The pulp cords contained erythrocytes and the pools were accounted for by these distended pulp cords no evidence of reverse flow of erythrocytes from the pulp cords into the arterial capillaries was present. It appeared that the perfused fluid carried the erythrocytes from the larger veins back into the smaller venous sinuses then the fluid escaped from the venous sinuses into the pulp spaces through the stomata and then into the arterial capillary endings in the pulp cords washing out the erythrocytes originally present in these capillaries. No abnormalities were demonstrated in the arterial capillary terminations or ampullae and no pools were produced in the venous sinuses despite the reversal of the circulation.



daily for two to three weeks for the most part although reticulocytosis was observed after even a single dose by mouth, larger doses of about 100 mgm. were given daily for 19 to 38 days. Diets were regulated carefully so that the source of extrinsic factor would be minimal.

Thirteen of the patients showed a positive haematological response consisting of reticulocytosis and subsequent rise of erythrocytes haemoglobin and leucocytes and in cases where treatment was continued the regeneration progressed to normal levels the responses to treatment paralleling those afforded by potent liver extract. In addition a feeling of subjective improvement occurred between the third and fifth days of treatment before the day of the initial reticulocyte response the symptoms were also improved diarrhoea disappeared, glossitis cleared, while the paraesthesiae of combined system disease were partially relieved. Further studies have shown that synthetic folic acid is effective in treatment of the macrocytic anaemia of sprue pellagra, and pregnancy it had no effect on anaemia due to iron deficiency on several types of anaemia associated with hypoplastic bone marrow and on "myelophthisic" anaemia due to aleukaemic myelogenous leukaemia.

F Murgatroyd

PAREYRO P. Contribución de la citología en el diagnóstico de las afecciones de la sangre y de los órganos hematopoyéticos. Cytology in Diseases of the Blood and Blood-Forming Organs. *An. Facul de Med de Montevideo*, 1945 v 30 Nos. 9 10 & 11, 612-643, 142 figs (1 coloured) [Bibliography]

## VENOMS AND ANTIVENENES

FINLAYSON, M. H. & HOLLOW, K. The Treatment of Spider Bite in South Africa by Specific Antivena. *South African Med J* 1945 Nov 24 v 19 No. 22, 431-3.

The chief cause of venomous spider bite knoppe bite in South Africa is the *Latrodectus* either *L. indistinctus* or *L. geometricus*. Antivenenes against the former prepared from goats have been found effective in bites by the latter also. R. H. N. SMITHERS thinks that *L. indistinctus* is a colour variety of *L. tredecimguttatus* (of Southern Europe) and both *L. indistinctus* and *L. mactans* may be but variants of *L. tredecimguttatus*.

The authors have tested in mice the action of an antivenene against *L. mactans* the Black Widow spider obtained from the Argentine first against *L. indistinctus* venom and they found that 1 cc. of anti-*mactans* serum would protect the mice against 1,200 m.l.d. of the *indistinctus* venom (0.25 cc. of 1 in 60 dilution of the antiserum gave complete protection against 5 m.l.d. of the *indistinctus* venom). Next, the protective action of the same antivenene, injected intravenously in a dose of 0.2 cc. of a 1:5 dilution was tested when given 25 hours after intramuscular injection of *indistinctus* venom. All the mice survived, but two controls died in 28 and 32 hours respectively. Lastly protection against the bite of *L. indistinctus* was tested, 0.25 cc. of 1:20 dilution of the anti-*mactans* serum being injected immediately after the bite. All the mice lived, whereas a control died in 17 minutes. Whether the action is reciprocal i.e. whether *L. indistinctus* antivenene will protect against the effects of *L. mactans* bite has yet to be proved and until this is done it cannot be affirmed that the venoms of *L. indistinctus* and *L. mactans* are identical.

H Harold Scott

BELL J E Jr & BOONE J A Neostigmine Methylsulfate an apparent Specific for Arachnidism (Black Widow Spider Bite) *J Amer Med A*  
1945 Dec 8 v 129 No 15 1016-17

- 1 In a typical case of arachnidism the symptoms failed to respond to calcium gluconate and sedatives for a period of five and one half hours
- 2 Dramatic and complete relief of muscle spasm and pain followed within one hour the intramuscular injection of 2 cc of 1/2 000 neostigmine methyl sulfate with 1/150 grain of atropine sulfate
- 3 This single case is presented in the hope that this apparently specific therapy will be tried in other cases without delay

### DERMATOLOGY AND FUNGUS DISEASES.

WOLFE W D Diseases of the Skin among the Natives of Northeast New Guinea. *Arch Dermat & Syph* 1945 Oct v 52 No 4 247-8.

- 1 The dermatologic abnormalities in a group of 1 047 natives of north east New Guinea are tabulated and discussed briefly
- 2 The most frequently encountered cutaneous diseases were scabies ulcers and tinea these comprised 80 per cent of all diseases of the skin noted.
- 3 With the exception of yaws tinea unbricata filariasis and keratoma plantare sulcatum the type of cutaneous disease found among the natives differs little from that seen in the United States

MARPLE C D Progressive (Disseminated) Coccidioidomycosis Report of a Case.  
*Ann Intern Med* 1945 Aug v 23 No 2 240-49

### HEAT STROKE AND ALLIED CONDITIONS.

SAPHIR W Chronic Hypochloremia simulating Psychoneurosis *J Amer Med Ass* 1945 Oct 13 v 129 No. 7 510-12.

Ten cases are described with ill-defined intestinal and nervous symptoms resembling those of psychoneurosis. The blood in all ten cases was found to be deficient in chloride i.e. it contained less than 400 mgm per 100 cc. (63-4 m eq/L). The patients rapidly improved when given a regular diet with vitamin supplements and extra salt and the blood chlorides rose to the normal level. The author considers that all these men were suffering from chronic hypochloremia [although some of the improvement may well have been due to the vitamin supplements and rest]. The patients had been in the tropics for periods varying from 3 weeks to nearly 31 months [it is not stated whether they had lost weight in this time]. The author suggests that these men had not taken enough salt to prevent a gradually increasing chloride deficit though they had taken enough to prevent heat exhaustion consequent upon a sudden call on body salt and he draws attention to the possibility that chronic hypochloremia may be missed if it is not specifically looked for.

H S S Ladd.

macules and vesicles on the trunk and limbs and a few similar lesions on the external genital organs. His temperature was about 102°-103°F for a few days but soon subsided, and he recovered in rather over one week.

The authors regard the lesions of the mucous membranes as the most important part of the disease causing the fever and the severe local discomfort.

J. F. Corson.

MORANTY J. H. The Presence of Rhinocleroma in Kerapot District of Southern Orissa. *Indian Med. Gaz.* 1945 Sept. v 80 No. 9 458-9

Report of one case.

GRING, E. D. W. On Tropical Eosinophilia associated with Pulmonary Signs (Loeffler's Syndrome) *J. Trop. Med. & Hyg.* 1945 Dec.-1946 Jan. v 48 No. 6 149-51 27 refs

HAWKING F. The Choice of Sulphonamides. *Practitioner* 1946 Jan. v 156 No. 831 72-3 [Summary appears also in *Bulletin of Hygiene*.]

In this short note Hawking includes a table which, because it summarizes so clearly the sulphonamides suitable for the treatment of certain diseases will be valuable to readers of this *Bulletin*. It is a condensation of the information contained in the Medical Research Council War Memorandum on the Medical Use of the Sulphonamides (see this *Bulletin* 1945 v 42, 1052)

Table showing which sulphonamides to use in different conditions

Condition	Sulphonamide
Haemolytic streptococcal infections (moderately severe)	Sulphamylamide.
Haemolytic streptococcal infections (severe)	Sulphathiazole sulphadiazine or sulphamerazine.
Otitis media	
Meningococcal meningitis	
Purulent meningitis	
Pneumonia	
Staphylococcal infections (if penicillin is not available)	
Chancroid	
Lymphogranuloma inguinale	
Peritonitis (for insertion after operation)	
Gonorrhoea (if penicillin is not available)	
Urinary infections	Sulphathiazole or sulphamerazine.
Wounds and burns (local applications)	Sulphathiazole, sulphamylamide or mixture of the two
Bacillary dysentery	Sectinylsulphathiazole sulphaguanidine or sulphadiazine
Prophylaxis against meningococcal infections or rheumatic fever	Sulphadiazine sulphamerazine or sulphamylamide.

Charles Wilcocks

DAVALOS A. The Rarity of Stones in the Urinary Tract in the Wet Tropics  
*J Urolgy* 1945 Aug v 54 No 2, 182-4 [16 refs]

The observations recorded in this paper were made in some of the tropical regions of Ecuador South America. In certain areas of that country particularly on the west coast and in the south, urinary lithiasis is of very rare occurrence during a year of urological practice in the southern part of Ecuador the author did not see a single case among 60 000 persons examined.

The diet of the people of tropical Ecuador is poorly balanced and deficient in protein and vitamins especially vitamin A. The large quantity of bananas eaten produces high acidity of the urine. In northern Peru where urinary lithiasis is common the diet is similar but the climate there is warm and dry throughout the year while in Ecuador it is hot and humid.

The average pH of the urine of 500 patients was 5.0. Cultures of their urine were all negative for the common urea splitting organisms (*Proteus vulgaris* and others).

The author concludes that the rarity of urinary lithiasis in certain parts of Ecuador is attributable to the fact that the profuse perspiration caused by the climate reduces the eliminatory strain on the kidneys and the low urinary pH by inhibiting the growth of urea splitting organisms prevents the precipitation of phosphates and carbonates in the urinary tract. The rare cases of lithiasis found are due to uric acid or cystine.

J F Corson

LEITNER A J. Le cancer en Côte française des Somalis [Cancer in French Somaliland.] *Bull Soc Path Exot* 1945 v 38 Nos 7/8 235-41

The author gives a tabular list of malignant growths observed radioscopically and at post mortem examination in natives of French Somaliland, during the years 1939-43. The total number was 24 and included primary cancer of the liver (8) cancer of the pancreas (1) cancer of the rectum (1) cancer of the stomach (2) cancer of the oesophagus (1) cancer of the tongue (3) cancer of the breast (1) epithelioma of the ear nose jaw skin of the shoulder and skin of the abdomen one each a mixed tumour of the parotid and a connective tissue tumour of the thigh. Short notes of four cases of primary cancer of the liver are given and a few cases of various malignant growths in non-natives are mentioned.

J F Corson

## GENERAL PROTOZOOLOGY

NERY GUIMARÃES F. Toxoplasmose humana. Meningoencefalomielite toxoplasmica. ocorrência em adulto e em recém-nascido [Human Toxoplasmosis. Toxoplasmic Meningoencephalomyelitis in an Adult and an Infant.] *Mem Inst Oswaldo Cruz* 1943 June v 38 No 3 257-320 2 pls (1 coloured) 1 map 28 figs & 2 graphs [65 refs] English summary

This is a long paper largely taken up with a historical summary of our knowledge of toxoplasmosis up to 1942. It is based on two cases seen in Brazil the one in a young man 18 years of age and the other in an infant 14 months old. Both cases were fatal and it was possible in the case of the adult to carry out a detailed histopathological study. This revealed a meningoencephalomyelitis characterized by extensive inflammatory areas with or without necrosis in the white and grey matter of the brain. Scattered through the tissues were miliary and submiliary granulomata usually situated in relation

to blood vessels. Inflammatory areas were seen in the myocardium while necrotic foci occurred in the liver and hypophysis. Typical parasites were seen in smears and in sections. They were intracellular in pseudocysts or free.

The disease in the infant was characterized by hydrocephalus with areas of intracerebral calcification, associated with tremors and convulsions. Diagnosis was established by the infection produced in animals by inoculation of cerebrospinal fluid.

The paper is illustrated by a number of microphotographs and a coloured plate showing the character of the parasite isolated. C. M. Wenyon.

BRUG S. L. & Vos J. J. T. *Toxoplasmosis hominis*. Reprinted from *Nederl Tijdschr v Geneesk.* 1942, Nov 28 v 86 No. 48 2956-63 47 figs. on 1 pl English summary

Review of the most recent literature on human toxoplasmosis. Further anatomical and parasitological details on the case observed in Groningen. In this case the sections of the brain contain parasites which were obviously multiplying by schizogony."

I. WATSON J. M. The Identity of the Ciliate *Balantidium minimum* an Alleged Parasite of Man. *Trans. Roy Soc Trop Med. & Hyg.* 1945 Oct. v 39 No 2, 151-60 4 figs. [20 refs.]

II. — Observations on the Coprophilic Habits of a Ciliate *Balantrophorus minimum* Schewiakoff. *Ibid* 161-5. [12 refs.]

i. In the first paper the author reviews the records of the discovery of *Balantidium minimum* in human faeces since SCHAUDINER first described it as a human parasite in 1899. Several writers have held that the ciliate was probably not a parasite, but a coprophilic organism which is liable to contaminate stools and that its presence has led to erroneous conclusions regarding its parasitism. The author has made a careful study of the various descriptions of the ciliate and has come to the conclusion that it is *Balantrophorus minimum* Schewiakoff, a free-living ciliate which, under certain conditions may live and multiply enormously in human faeces after they have left the body.

ii. In the second paper are given the results of an investigation into the factors which favour or inhibit the development of *Balantrophorus minimum* in human faeces. In normal stools active multiplication may occur leading to fantastic abundance of the ciliates. In abnormal stools from various sources whether loose, diarrhoeic or dysenteric, there was usually not only a failure to develop but rapid extinction occurred. The reasons for this were found to be the presence of urine, bile salts or traces of drugs and conditions of high osmotic pressure. It was determined by experiments on mice that cysts of the ciliate were unable to survive passage through the intestine. Faeces of mice fed on cysts when emulsified in water failed to yield cultures of the ciliate which, however developed vigorously when inoculated directly into such faecal emulsions. *Balantrophorus minimum* is a soil protozoan and as such is capable of living in an amoeboid form in mere surface films of water and is capable of surviving a considerable degree of drying in the unencysted state. These qualities enable it to live and survive in the viscous semi-solid material of a stool in which any ordinary ciliate would rapidly succumb. This does not mean that an organism of this type is capable of living in the human intestine. In fact, it has never been proved that any free-living protozoan can enter the intestine of a warm-blooded animal in the encysted stage and emerge from the cyst to survive or multiply in some part of the intestine. In the supposed

infections with *Balantidium minutum* it seems clear that the stools after being passed became contaminated with airborne cysts or water-borne free-living forms of *Balantophorus minutus*

C M Wenyon

## GENERAL ENTOMOLOGY

BATES M Observations on Climate and Seasonal Distribution of Mosquitoes in Eastern Colombia. *J Animal Ecology* 1945 May v 14 No 1 17-25  
1 pl. & 3 figs [13 refs]

This area of Eastern Colombia (S America) has a remarkably uniform climate with only 2.8°C difference between the mean temperature of the hottest month (February 27.8°C) and of the coolest (July 25.0°C). There is a greater variability in rainfall though even in the driest month (February) there is usually more than 3 in (87 mm) of rain. May is the wettest month with 28 in. (690 mm.) the annual precipitation is 180 in. (4 645 mm). Even in the driest month the noon relative humidity does not fall below 60 per cent.

Most attention in this investigation was paid to *Haemagogus capricornis* a probably important vector of jungle yellow fever but other species of mosquitoes were also studied. Diurnal captures were made by men standing in various locations and catching all mosquitoes that came to bite. Nocturnal species were caught in a stable trap baited with a donkey.

*Haemagogus capricornis* was by far the commonest diurnal mosquito accounting for nearly 80 per cent of those captured. *Anopheles rangeli* comprised over 50 per cent. of the nocturnal catch.

Most species were scarcest in March i.e. at the end of the dry season. They then reached a maximum about June and fluctuated for the remainder of the year. The reasons for these fluctuations are discussed.

Kenneth Mellanby

ROUBAUD E. & COLAS-BELCOUR J Influence de la salure des eaux sur le développement de l'*Aedes aegypti*. [Influence of Salinity of Water on the Development of *Aedes aegypti*] *Bull Soc Path Exot* 1945 v 38 Nos. 5/6 136-45 [12 refs]

In a large series of experiments gravid female *Aedes aegypti* were given water of five different salinities ranging from tap water (containing only 0.146 gm. NaCl per litre) to full strength sea water in which to oviposit. The 17 940 eggs laid in all these experiments were distributed as follows: tap water 28.9 per cent of the total eggs; tap water plus 31 per cent sea water 28 per cent; tap water plus 42.6 per cent sea water 22 per cent; tap water plus 62 per cent sea water 17.8 per cent; sea water 3.1 per cent.

Observations on the activities of the insects revealed that non-gravid and gravid females alike (and also males) were equally attracted to all these five samples of water. Egg laying is soon discontinued in the strong saline solutions the saline concentrations being apparently detected by the posterior extremity of the abdomen which comes into contact with the water-surface during oviposition.

Kenneth Mellanby

BELKIN J N *Anopheles nataliae* a New Species from Guadalupe. *J Parasitology* 1945 Oct. v 31 No 5 315-18 6 figs on 1 pl

KENNEY M. Experimental Intestinal Myiasis in Man. *Proc. Soc. Exper Biol & Med* 1945 Nov., v 60 No. 2, 235-7

"From 60 volunteers fed with living maggots of *Musca domestica* Calliphora, and Sarcophaga under conditions to avoid their destruction in the stomach, only 10 failed to have symptoms of gastro-intestinal disturbance.

In 50 cases men had nausea, vomiting, intestinal cramps and diarrhea together or as separate symptoms but all symptoms disappeared within 48 hours following the elimination of the larvae of which only a few were found alive in the vomitus and stools.

"These findings seem to indicate that though temporary gastro-intestinal distress may follow the ingestion of such dipterous larvae as *Musca domestica* Calliphora and Sarcophaga they do not produce a true intestinal myiasis in man.

BEAMENT J W L. The Cuticular Lipoids of Insects. *J Exper Biol* 1945 Aug v 21 Nos. 3 & 4 115-31 7 figs [31 refs]

POWING R. F. The Analysis of D.D.T. and Pyrethrins in Kerosene-based Sprays. Reprinted from *J Council Scient. & Indust Res* 1945 May v 18 No. 2 121-3.

A method developed for the separation and analysis of DDT and pyrethrins in a mixed insecticide spray is described. *J R Bussinc*

## LABORATORY METHODS.

HAY S. Despatch of Material for Histological Examination. *Edinburgh Med J* 1945 Nov v 52, No. 11 428-9

Correct treatment of tissue before posting it to a laboratory for histological examination is specially important in the case of biopsy tissue. The three main injunctions are (1) put it at once into fixative without previous washing in water (2) do not cut into it (3) send it without delay. The best general fixative is a mixture of formalin with 9 parts of tap water.

Biopsy material may be (1) large such as a breast with the glands (2) medium-sized, such as an encapsulated tumour and (3) small such as uterine curettings. In the case of large material if the surgeon wishes to see the type of lesion he should not gash it irregularly but should make one planned cut in the most suitable axis not quite through the whole but so as to leave a hinge so that the whole can be closed up again. Medium-sized material should be at least  $\frac{1}{2}$  to  $\frac{3}{4}$  in. thick and should be cut in the best direction to include all tissues affected and healthy including an advancing margin and a diagnostic part. If the specimen is too large for despatch in fluid, it may be wrapped in formalin-soaked cloth covered by "Cellophane" or gutta-percha tissue. Small material such as uterine curettings should be put into a small linen bag (not a gauze bag) in the fixative to avoid any loss.

In all cases freshly removed tissue should never be placed on dry gauze as this has a powerful desiccating capillary effect.

Bottles should be nearly full as a large volume of air tends to injure the specimens. They should, of course be securely sealed and packed, and notes should be enclosed. *J F Corson*

# TROPICAL DISEASES BULLETIN.

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## SUMMARY OF RECENT ABSTRACTS.\*

## IV TRYPANOSOMIASIS

## AFRICAN TRYPANOSOMIASIS.

*Epidemiology*

MACKICHAN (p 13) reports an outbreak of human sleeping sickness in Uganda in which during the period 1940-1943 there were 2,432 known cases and 274 deaths. The outbreak was declining when the author wrote the paper. Clinical and experimental evidence indicated that the trypanosome concerned was *T. rhodesiense* and the author states that this organism has not apparently been isolated previously in Uganda [but DUKE (p 13) writes that it was found several years ago]. One of several volunteers was infected with trypanosomes which were passed through rats from wild-caught *Glossina pallidipes*. The outbreak was probably due to the introduction of infection by labourers brought from Tanganyika Territory.

CECCALDI (p 710) reports on sleeping sickness in French Equatorial Africa.

*Actiology*

VAN HOOFF *et al* (p 96) quote the arguments which support the view that *T. gambiense*, *T. rhodesiense* and *T. brucei* are biological races of a single species rather than independent species. To distinguish between them these authors have studied the forms present in the salivary glands of infected tsetse flies and have concluded that the distribution, relative numbers and dimensions of the various developmental forms in the salivary glands provide a ready means of differentiation between *T. gambiense* on the one hand and *T. rhodesiense* and *T. brucei* (which are indistinguishable) on the other. These differences are set out in tabular form for which the original abstract should be consulted. In comment, HOARE remarks that since the differences between the two subgroups are purely relative, the three species of polymorphic trypanosomes must still be regarded as morphologically identical and he notes that certain facts mentioned by the authors appear to be contradictory.

STEFANOPOULO and ÉTÉVE (p 258) have shown that a strain of *T. gambiense* previously reported by ROUBAUD and PROVOST to have neurotropic properties

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945 v 42. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.



for mice does in fact, produce meningo-encephalo-myelitis in these animals. It had previously been thought that mice showed blood infection only.

RODHAUX and VAN DEN BERGHE (p. 872) have succeeded in infecting chick embryos with certain spirochaetes, leishmania and trypanosomes. Most of the pathogenic organisms grew in the embryos but all the non-pathogenic organisms failed to do so.

#### TRANSMISSION.

BAX (p. 702) reports on the work of the Tsetse Research Department (Tanganyika Territory) since February 1944. The items of work done are too numerous to be recapitulated here, and the original abstract should be consulted for details. Mention may however be made of an attempt to oust *G. swynnertonii* by introducing into its habitat large numbers of pupae of *G. morsitans*. The latter fly soon outnumbered the former and some hybrids were caught but it is too soon to know if the experiment was successful.

POTTS (p. 89) reports an attempt made at cross-breeding between *G. morsitans* and *G. swynnertonii*. A few hybrids were obtained, and some of these hybrids (females) were fertile after insemination by *G. morsitans* or *G. swynnertonii*. Further matings did not produce offspring. Cross-mating seems to occur less readily than mating within the species [but see VANDERPLANK, below] but the evidence suggests that the introduction of large numbers of pupae of an alien species into country where the indigenous species is not plentiful may lead to cross-mating and the production of relatively few and infertile offspring. This is a possible method of tsetse control. VANDERPLANK (p. 99) gives a table of the cross-mating which he has effected between *G. morsitans* and *G. swynnertonii*. Insemination occurred as readily in the cross-matings as with the same species where no choice was offered, but the cross-matings produced far fewer pupae. The author brings out the point that a few hours after a female is inseminated "she is no longer attractive to males and will not permit further coitus."

JACKSON (p. 188) has continued his observations on a *G. morsitans* population and has confirmed his finding that dispersal consists largely of movement within ambits governed by vegetational boundaries which are rarely more than half a mile in radius. It appears that a catch of one "old" male fly per 10 000 yards represents a population of some  $7\frac{1}{2}$  "old" males per square mile and perhaps twice as many females. The author discusses the factors which bear on these conclusions and which must be taken into account in computing results.

CHORLEY (p. 98) has found *G. palpalis fuscipes* breeding as far as 12 miles from water in dense humid forest broken up by elephant tracks. He thinks that the general limitation of the fly to waterside areas is determined, not by food supply (which exists elsewhere) but by climatic conditions of shade and humidity.

In the Uganda outbreak MACKICHAN (p. 13) found three species of *Glossina* — *G. pallidipes* (the chief if not the only vector in the area) *G. palpalis fuscipes* (which breeds in evergreen forest as far as 10 miles from water) and *G. brevipalpis*.

WILLIAMS (p. 14) in one small experiment in Portuguese East Africa found that *G. pallidipes* was most active in the evening and early morning. BURTT (p. 888) shows that *G. pallidipes* which have hypertrophied salivary glands appear to be particularly suited to the development of trypanosomes especially *T. brucei*.

JACKSON and VANDERPLANK (p. 187) have measured the diameters of red blood cells of about 40 species of East African mammals. There is considerable difference between species but closely related species have cells of about

the same size. The work was done in relation to the animals on which tsetse flies feed.

POTTS and VANDERPLANK (p 869) give their reasons for the opinion that contact insecticides (pyrethrum and DDT) are absorbed through the pulvilli of tsetse.

GASCHEN (p 453) has written a monograph on the tsetse flies of French West Africa.

#### *Clinical Findings*

In a description of sleeping sickness as it is seen in Tanganyika Territory FAIRBAIRN (p 452) makes the point that this infection (by *T. rhodesiense*) can always be diagnosed by blood examination that gland puncture is unnecessary but that in some advanced cases diagnosis can be made more quickly by lumbar puncture. Prognosis depends greatly on the protein content of the cerebrospinal fluid and can be estimated from observations made over a period of some months. Treatment with Suramin (Bayer 205) need not be stopped on account of albuminuria but vision should be tested before each dose of trypanamide. In relapses repeated courses of trypanamide should be avoided because of the danger of making the trypanosomes arsenic fast and because of the risk of producing optic atrophy. Monthly doses of Suramin may be given to keep the blood free from trypanosomes. The author argues against the use of Suramin as a prophylactic since there is a real danger of cryptic infection it is preferable for the individual to get a definite attack which can easily be diagnosed and cured.

A case of Gambian sleeping sickness in a British soldier who had served in Nigeria some years before is reported by GRANT *et al* (p 187). The diagnosis was not made until 2½ years after the probable time when the infection was contracted. This case illustrates the difficulty of diagnosis sometimes experienced in this infection and points to the importance of keeping in mind the possibility of sleeping sickness in returned soldiers. Referring to the paper by Grant *et al* above and to the diagnostic methods that had been used by the various medical men who had examined the patient HARDING and HAWKING (p 188) show that the well-known procedure of gland puncture might have been used with advantage and that blood culture is a simple and practical method which may give positive results when other tests are negative.

FAIN (p 14) found trypanosomes in material from sternal puncture in 11 of 20 patients with clinically advanced disease but in whom blood and gland juice (except in one instance) were negative. This method of examination is therefore useful.

SIEYKO NIETO (p 15) has made investigations on the blood picture the coagulation time the serum calcium and on various tests with the cerebrospinal fluid in trypanosomiasis as it was seen in Fernando Po. For the last he thinks the cell count more useful than the total protein figure but there may be an abnormal colloidal gold reaction in the absence of abnormal cell count or total protein and thus may be the only sign of involvement of the central nervous system.

VAN GOIDSENHOVEN and SCHOENAERS (p 791) describe the preparation of an antigen suitable for the complement fixation test in trypanosomiasis.

RODHAIN and VAN GOIDSENHOVEN (p 889) have shown that the complement fixation test (in which an antigen prepared from *T. equiperdum* is used) tends to remain positive in man and in animals for some years after clinical cure. A positive test is not an indication for the continuation of treatment.

#### *Treatment*

FOWLER (p 541) has treated 42 cases of Gambian sleeping sickness with trypanamide administered by intravenous drip the dose being 2 gm. daily

(in 2 pints of double-distilled water which take 8 hours to give) for 6-8 days with an interval of one day in the middle of the course. This treatment causes high fever and exhausts the patients. It may have been partly responsible for death in the seven subjects who died. Nevertheless in spite of the fact that there was evidence of involvement of the central nervous system in most of the patients the immediate results were good in those who survived and in patients observed for several months the improvement was maintained.

EAGLE (p. 354) reports that  $\gamma$ -(p-arsenosphenyl)-butyric acid has been tried in human sleeping sickness in West Africa, and that the results in early cases are satisfactory, cure being achieved within two weeks by daily injections of about 0.4 mgm. per kgm. body weight. It is ineffective in late cases and may cause toxic encephalitis in such patients.

KING (p. 971) discusses the chemical structure of arsenicals and drug resistance of trypanosomes. The paper is highly technical, and details should be sought in the original abstract.

HAWKING (p. 971) has found that at 37°C living trypanosomes absorb a large amount of stilbamidine but that dead trypanosomes do not absorb it in any appreciable amount. Evidence was obtained that trypanosomes in the blood of animals absorb the drug *in vivo* when it is injected into the animals. SAUNDERS *et al.* (p. 354) have followed up a number of patients with Gambian sleeping sickness treated with pentamidine. The results suggest that those whose cerebrospinal fluid contains less than 30 cells per cmm. are usually cured but that in those with more than 30 there is usually relapse. In very advanced cases the drug is useless.

### Control

In a paper on recent progress in the control of sleeping sickness in Nigeria LESTER (p. 789) makes the point that the disease assumes different forms—mild, toxic or nervous—and that the mild form is the most common. At the height of the epidemic some years ago teams were formed to give mass treatment, but the author thinks that where the incidence of the disease is reduced to about 1 per cent. the permanent treatment centres now established will be in a position to detect any outbreak and to deal with it. Great success has attended the work of the mass treatment teams. River clearing has been successful in eliminating the riverine tsetse from large areas and the Anchau corridor of 490 square miles is now free from fly.

In the report on the medical services of Nigeria for 1943 (p. 790) it is stated that there was no evidence of any general increase of sleeping sickness in that year. At the permanent treatment centres not only sleeping sickness but other diseases also are dealt with.

HUNT and BLOSS (p. 969) state that sleeping sickness has never been eliminated from part of the Sudan which adjoins French territory. They have attempted control by instituting a modification of SYMES's block method, to deal with *G. palpalis fuscipes* the only vector. This has been very successful. BLOSS (p. 969) describes an outbreak of sleeping sickness near Mendi in the Sudan, which was controlled by the block method and by the creation of rod clearings along the streams haunted by *G. palpalis*. Each method possesses its own advantages. He found that the disease could establish itself even where the fly density was low and contends therefore that fly control must be thorough. The infection was of the Gambian type.

### TRYPANOSOMIASIS OF ANIMALS.

#### General

BROWAETS (p. 189) has infected mice with single trypanosomes from a strain of *T. brucei* maintained in Paris. The incubation period was usually

longer than when several trypanosomes were injected, but the duration of the disease was not apparently related to the dose

FIENNES *et al* (p 791) describe the course and pathology of *T. congolense* disease of cattle. VANDERPLANK (p 703) has succeeded in infecting *G. longi pennis* and *G. fuscipennis* with *T. congolense* and has found one female *G. austeni* infected in nature with the same trypanosome

KUBES (p 454) has written a monograph in which he compares Venezuelan and African strains of *T. vivax*

SEAGER (p 261) has succeeded in infecting ducks by injection of *T. equiperdum* and refers to the possibility that there may be avian reservoirs of similar mammalian parasites. In comment CORSON states that human and other mammalian pathogenic trypanosomes have successfully been transmitted to various species of birds and that avian blood has been found in nature in tsetse flies. CHEN *et al* (p 872) report observations on parasitaemia and length of survival of mice infected with *T. equiperdum*

VAN DEN BERGHE (p 871) has investigated the infection of chick embryos with *T. evansi* for details the original abstract should be consulted.

ROMANA (p 873) reports on the infection of bats with *S. vespertilionis*

#### *Treatment.*

CALVER (p 704) has written a thesis (unpublished) on chemotherapeutic studies in experimental *T. congolense* infections. This has been very fully abstracted. Two strains of the trypanosome were used which differed in pathogenicity and in the course of the infections they produced. The author distinguishes between acute strains (passed from mouse to mouse at the point when the trypanosomes first become uncountable in the blood) and relapse or chronic strains (passed at a later stage of the infection). Treatment was given at various stages of the disease and for this the author used certain compounds of the phenanthridinium series Stilbamidine and quinoline methochloride. The details of these treatments cannot be summarized more satisfactorily than in the original abstract the results indicate considerable value for several of the compounds tested. Attempts to produce drug fastness were not successful. The immunity developed after infection and cure differed in the two strains and was complex even in relation to the homologous strain there was no cross-immunity between the strains. Field trials in Africa with two of the phenanthridinium compounds have been reported, and these together with the author's own work indicate that the drugs are likely to be useful. BROWNING *et al* (p 258) have found that one of the series of phenanthridinium compounds has a curative action in *T. congolense* infections of mice at a dosage much less than the maximum tolerated dose. BROWNING and CALVER (p 259) have taken this work further using two strains of *T. congolense* with somewhat different characters. Treatment was more effective when the trypanosomes were abundant than earlier which suggests that immunity may play a part in the cure. Immunity after cure was much more solid with one strain than with the other and there was no cross immunity. In the field results may depend on the strains of *T. congolense* the stage of infection and other factors. CARMICHAEL and BELL (p 259) have tested this drug in *T. congolense* infections of cattle and advise that it should be given intravenously or intramuscularly. Most of the animals relapsed but retreatment was largely successful. Details are given in the original abstract.

A new phenanthridinium compound prepared by BROWNING was tested in cattle infected with *T. congolense* by CARMICHAEL and BELL (p 260) in Uganda. The results were very good, and cure was obtained in all cases. The subcutaneous route of administration is apparently favoured and though toxicity was not investigated it is believed to be low.

var *atroparvus* and *A. sacharovi* (the last two on epidemiological grounds). Finally there is a key designed to facilitate the identification of Chinese anophelines

Norman White

HUFFAKER, C. B. SOTO H. & REY H. Additional Wild-Caught *Anopheles punctimacula* D and K. infected with Malaria Plasmodia in Colombia, South America. *Amer J Hyg* 1945 Sept. v 42, No. 2 107-10. [12 refs.]

The scanty evidence upon which was based the conclusion that *Anopheles punctimacula* D and K is "incapable of transmitting malaria," is briefly mentioned. It amounts to failure to demonstrate malaria plasmodia in 18 mosquitoes after feeding on infected persons.

Since 1938 three natural infections have been reported the present authors record five more. In February 1944 they collected adults from houses and in June the same year from houses stables and baited traps. They supplied the females with 10 per cent. sucrose and kept them alive at 72°F for from five to eight days before dissecting them. The stomachs only were then removed and stored in 50 per cent. alcohol until they could be stained and examined.

In three stomachs very small cysts were seen which would easily have been missed if the females had not been kept alive for some time after capture. Altogether out of 433 stomachs five were found to be infected (1.2 per cent.) but these all occurred in the June dissections (326) which gives an infectivity rate of 1.5 per cent.

The authors conclude that *Anopheles punctimacula* must not be ignored as it may be a dangerous vector of malaria wherever it is produced in abundance.

H S Lesson

ROGERS K. B. Concentrating Malaria Parasites in Thin Films. *Brit Med J* 1946 Jan. 5 11-12.

The author describes a technique which he has devised for concentrating malarial parasites for the purpose of facilitating diagnosis. It involves centrifugation in a small tube followed by removal of the packed red cells and some serum in a capillary tube. This tube is centrifuged (2,000-3,000 revolutions) for 20 to 30 minutes. The top portion of the packed red cells is cut off with a little of the supernatant serum. This piece of capillary tube open at both ends is inserted into a specially constructed pipette which has an S-shaped bend to prevent the tube passing to the closed lower end of the pipette. The pipette with the tube in it is centrifuged for 2 to 5 seconds. The blood and serum are driven out of the capillary tube to the closed lower end of the pipette. On cutting off the tip of the pipette the red cells and serum can be blown on to a slide for film making. It is claimed that a concentration of from 5 to 56 times can be obtained. Of 52 positive bloods five were positive only in the concentrated blood film. Those interested in the technique must consult the original paper for further details

C M Wexson.

METCALF R. L. The Detection of the Plasmodia of Human Malaria in Blood Films by Fluorescence Microscopy. *J National Malaria Soc* Tallahassee Fla. 1945 Sept. v 4 No 3 223-9 3 figs.

The paper describes a method of identifying malarial parasites by means of the fluorescence microscope. Thin blood films fixed in methyl alcohol are stained with berberine sulphate or rivanol. When such films are observed under the fluorescence microscope the malarial parasites are luminous and are thus easily detected. It is claimed that the appearances of the three species

of parasite are much like those seen in Giemsa preparations except for the colour differences. The author suggests that because of its simplicity the method may be of value in routine malaria surveys. Similar observations have been made previously by BOCK and OESTERLIN and by PATTON and METCALF [this *Bulletin* 1944 v 41 545 and 546] C M Wenyon

SHUTE P G *Diagnosis of Malaria* Notes on the Preparation and Staining of Thin and Thick Blood Films, for the Detection of Malarial Parasites *Monthly Bulletin of Ministry of Health & Emergency Pub Health Lab Service* (directed by Med Res Council) 1946 Feb v 5 32-6

KLEEBERG J *Studies on the Weltmann Reaction in Malaria Cases* *Trans Roy Soc Trop Med & Hyg* 1945 Dec v 39 No 3 221-8 1 fig [36]

The Weltman Coagulation Reaction is an entirely unspecific protein-globulin reaction but the author considers that it might be of considerable diagnostic value in tropical fevers. The test consists in the addition of 0.1 cc. of haemoglobin free serum to each of a series of ten small test tubes containing graduated ascending dilutions of calcium chloride solution. The tubes are shaken and placed in a boiling water bath for 15 minutes. The reaction is then read. The contents of the tube may be clear faintly opalescent turbid or there may be flocculation. The number of tubes in which flocculation occurs is called the coagulation band. In normal serum the first six tubes usually show flocculation. Coagulation values of 6 or 7 are normal. If coagulation occurs in tubes with higher dilutions of calcium chloride (tubes 8 9 10) this shift to the right of the coagulation band is indicative of a chronic proliferative process. If there is a shortened coagulation band (tubes 1 to 5 only) such shift to the left is indicative of an acute inflammatory exudative process. The author reports on the results of the test in 25 cases of malaria. Though a malaria attack clinically produces all the features of an acute inflammatory process the W.C.R. showed a shift to the right in 13 cases was normal in 10 and a shift to the left in 2 only. Haemolysis may be responsible for the lengthened coagulation band in malaria. The test is particularly valuable in all haemolytic processes. It might be helpful in blackwater fever. The test repeated during the course of a disease may be helpful in prognosis. The test A succinct description of the technique is given.

Norman White

PLÖTNER, K. Ueber die Ursache der Regelmässigkeit des Malariafiebers [The Cause of the Periodicity of Malarial Fevers.] *Dent Tropenmed Ztschr* 1944 Apr-May v 48 Nos 7/10 148-56 5 figs

In three cases of malaria intercurrent infections which gave rise to continuous fever during the otherwise apyrexial periods between paroxysms resulted in the disappearance of the malarial fever and parasites.

In a patient suffering from quotidian paroxysms after subcutaneous administration of blood containing benign tertian parasites artificial fever was induced during an apyrexial period by intravenous injection of vaccine. After an apyrexial stage of two days following this artificial fever the periodicity of the malarial paroxysms became tertian and, according to the author, one generation of parasites disappeared from the peripheral blood. In two cases of sporozoite induced therapeutic benign tertian malaria however artificial fever had no effect.

The author suggests that an approximate 12 hour period of normal temperature is favourable to the development of *P. vivax* and *P. malariae*. Artificial

fever induction might be useful in conjunction with chemotherapy in frequently relapsing cases.  
B G Magnolia

LARA, P. \ Malarial Nephritis with an Illustrative Case Report. *J Indian Med Ass.* 1945 Nov., v 15 No 2, 48-7 & 43.

ANN TROP MED. & PARASIT 1945 Dec. 31 v 39 Nos. 3/4 157-8. Malarial Research leading to Paludrine. [Editorial.]

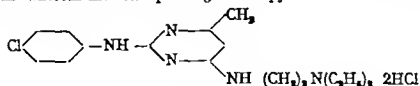
CURD F H S DAVEY D G & ROSE F L. Studies on Synthetic Antimalarial Drugs. I. Biological Methods. II. General Chemical Considerations. *Ann. Trop. Med. & Parasit* 1945 Dec. 31 v 39 Nos. 3/4 139-58 1 graph. [17 refs.] 157-64. [12 refs.]

In the Editorial Notice a brief outline is given of the researches leading to the synthesis of the new antimalarial drug Paludrine by the Imperial Chemical Industries Limited at Blackley Manchester and of the early clinical trials carried out by the Liverpool School of Tropical Medicine. This work owed a great deal to the initiative and vigour of the late Professor Warrington YORKE who gave much of his time to its welfare. The issue of the *Annals of Tropical Medicine and Parasitology* in which these researches are recorded is dedicated to his memory.

I In this paper written nearly two years ago the authors deal briefly with the life-cycle of malarial parasites from the point of view of chemotherapy in the light of recent knowledge resulting from intensive studies on bird malaria. Thus a drug may act on the sporozoite stage on the succeeding developmental forms named cryptozotes by HUFF *et al.* (this *Bulletin* 1943 v 40 515 1945 v 42, 538) and referred to as the tissue phase by DAVEY (this *Bulletin* 1944 v 41 365) or finally on the blood forms of the parasite, which are of most interest to the clinician. Whereas in the past drugs were tested against blood-forms, as in the well-known method of ROEHL, which is discussed, JAMES has long emphasized the need for a causal prophylactic which would be effective against the early stages of the parasite. It should not, however be forgotten that pamaquin and possibly mepacrine were discovered by Roehl's technique. Soon after the introduction of sulphonamides it was shown that certain members of the group had a degree of specificity against human malaria parasites which, however was not manifested against *P. relictum* by the Roehl test. The authors decided to use in their test acute *P. gallinaceum* infections in chickens on account of its practicability and the fact that this parasite was in line with the human parasites sensitive to certain sulphonamides as well as to the standard antimalarials, quinine pamaquin and mepacrine. Cross checks on activity were also made on *P. lophurae* infections in ducks and on *P. cathemerium* and *P. relictum* infections in canaries to determine any specificity of action. The erythrocytic forms found in *P. gallinaceum* infections did not interfere with the test for suppressive drugs on account of the acute nature of the treated infection. In the test which resembles that employed by American workers chicks six days old, were inoculated via a jugular vein with 0.2 cc. of a suspension of parasitized cells containing 40-50 million parasites, from a donor chick with acute infection. Parasites are demonstrable in the blood from the time of inoculation and a peak of parasitaemia occurs approximately four days later. In treating the established blood infection the drug was given orally by catheter in 1 ml. of fluid about 3 hours after inoculation and twice daily on the three following days. In order to assess the activity of an unknown drug comparison was made of the density of infections in six chicks treated with it, in six others treated with mepacrine whose potency was known, as well as

in the same number of untreated controls at the time when the peak of parasitaemia occurs in the latter. It emerged from the author's experimental work with mepacrine in agreement with earlier writers regarding quinine that there was a critical dosage range for this drug. A critical dose was established for each drug tested and compared with the standard mepacrine. The authors regard the critical dose as of the greatest importance it is defined as the minimum dose of a substance which administered according to a particular dosage schedule exerts what is materially the maximum effect of the drug. Other factors were also considered in the case of a new drug such as toxicity for mammals action against other plasmodia and possible specificity of action an interesting case of which is described before clinical tests were made on man. In this connexion their experiences with the drugs 2666 and 3349 (see below) are described. Whether a drug active in *P. gallinaceum* infection will be active in human malaria or whether different drugs given under a similar dosage schedule are absorbed to the same extent cannot be foretold. Nevertheless the test employed has led to the discovery of new and potent anti-malarials.

II The authors state their two main objectives to be the discovery of a true prophylactic drug in malaria and of other drugs more potent than existing types for use in clinical practice. The approach to the latter problem is described in this communication. Following the discovery of pamaquin and mepacrine which contain respectively a quinoline and an acridine nucleus synthetic work has centred mainly on derivatives of these types although other heterocyclic ring-systems have been studied. A drug more potent than mepacrine was not however discovered. The presence of basic side-chains attached to the different ring systems was shown to be of great importance for antimalarial activity by the work of SCHULEMANN and collaborators. The present authors have devoted their attention to certain derivatives of pyrimidine. Substances containing this ring-system are often of great physiological importance. Derivatives of molecular weight 300-400 containing a substituted phenyl group and basic side-chain were found to be inactive in *P. gallinaceum* infections whereas the corresponding anilino pyrimidines of which 2666



was an example showed antimalarial activity which persisted in spite of wide variations of the prototype. As stated by the authors. The prerequisite for antimalarial activity therefore appeared to be the simultaneous association with the pyrimidine nucleus of not only a basic alkylamino group but also an aryl group linked through a grouping capable of prototropic change. When the —NH— linkage of the above compound was replaced by a guanidine group —HN—C(=NH)—the compound 3349 (2-*p*-chlorophenylguanidino-4-β-diethyl-

$\text{NH}$

laminoethylamino-6-methylpyrimidine) was obtained which was active in bird malaria and the three common forms of human malaria when used as the dihydrochloride. This substance also offers possibilities of tautomeric change similar to those of 2666 above with which antimalarial activity may be associated a view which is discussed in relation to possible tautomeric changes in mepacrine. Certain views of others on the mode of action of this powerful antimalarial are given. The present authors believe that the pyrimidines 2666 and 3349 may undergo corresponding degradation changes *in vivo* and give



rise to compounds with marked similarities to riboflavin. Work is in progress to elucidate the mechanism of antimalarial action of these new substances and their possible relation to the yellow enzyme systems. J D Fulton

ADAMS A. R. D. & SANDERSON G. Studies on Synthetic Antimalarial Drugs.

III. A Preliminary Investigation of the Therapeutic Action of 3349 on Acute Attacks of Benign Tertian Malaria. *Ann Trop Med & Parasit.* 1945 Dec. 31 v 39 Nos. 3/4 165-8 IV. A Preliminary Investigation of the Therapeutic Action of 3349 on Acute Attacks of Malignant Tertian Malaria. *Ibid* 169-72 V. Further Investigation of the Therapeutic Action of 3349 on Benign Tertian and on Malignant Tertian Malaria Infections. *Ibid* 173-9 7 figs. VI. A Comparison of the Therapeutic Actions of 3349 and of Mepacrine Hydrochloride on Acute Attacks of Benign Tertian Malaria. *Ibid* 180-81 2 figs

III In view of the activity of compound 3349 in *P. gallinaceum* infections described above tests were now carried out in human malaria. The first trials were made on a strain of *P. vivax* which was employed in malaria therapy and had been passaged by blood inoculation. Such infections are easily cured. Five neurological cases were treated orally with 0.2 gm. of 3349 (see Part II) thrice daily on seven consecutive days while another case received half this amount of drug. The dosage was based on toxicity data for the drug in animals and it was believed to be not more toxic for mice than mepacrine. In all cases there was a rapid fall in temperature and disappearance of the parasite from the peripheral blood, with no marked evidence of toxicity. Infections with *P. vivax* in healthy males which had been acquired in different parts of the world were next treated. These infections were of several weeks or months' duration and most of the patients had been treated previously with standard antimalarials or had been given mepacrine prophylactically. All the patients were suffering from clinical malaria and had to be kept in bed. One man was experiencing his first severe clinical attack. Observations were made before treatment was started to verify that the attack was not ending spontaneously. Seventeen acute cases of naturally acquired benign tertian malaria were treated orally with 0.2 gm. of 3349 thrice daily for seven days. A thick blood film of each patient was examined daily while he was in hospital and twice weekly during convalescence. The clinical attack was in each case rapidly terminated by this treatment. Of seven other cases treated with half the dose three relapsed in 2-3 weeks three others remained well for 5-8 weeks while the seventh showed no response to the treatment but was clinically cured with the larger dose. There were no toxic symptoms with the smaller dose. Further courses of drug were given to some patients to find out if toxic symptoms occurred. One received 0.2 gm. of 3349 thrice daily on two consecutive days each week for 9 weeks and 15 others 0.1 gm. twice daily for periods up to six weeks. The only untoward symptoms encountered were mild colic and diarrhoea or frontal headache. There was a relapse in one case seven weeks after the first course while receiving 0.2 gm. of 3349 daily.

IV As the drug 3349 had shown activity in cases of benign tertian malaria treatment was now begun on cases of malignant tertian infection acquired in W. Africa or in the Mediterranean. Most of the men had been treated previously with standard antimalarials. The duration of the infections was from a few weeks to some months before treatment was begun but in some patients the first clinical attack of the disease was treated. The authors consider that it has not been clearly shown whether a primary attack of malignant tertian malaria in a patient who has had no prophylactic drug-treatment, or a delayed primary attack in one who has been so treated, is more responsive to chemotherapy than a patient suffering from relapse subsequent to previous courses

of treatment Their experience leads them to believe that the immediate response to an effective drug is similar in each case. No patients with infection of long standing were included in this study. The conditions for trial were the same as in Part III above. The clinical attack was successfully treated in 25 cases of malignant tertian malaria by 0.2 gm. of 3349 orally thrice daily for seven days. Nine of the patients were then discharged. In five others there was no relapse during a period of 3½ months. Two cases which relapsed in 3-4 weeks were retreated and responded to the above dosage whereas half the amount of drug proved unsatisfactory in curing clinical attacks or in preventing recrudescence. The remaining nine received a second course of 0.2 gm. of the same drug by mouth daily for 3-6 weeks and remained well and free from parasites during that period. The higher dosage caused slight colic and diarrhoea and transient headache in a few instances at the start of the treatment. In 15 cases of the same infection treated orally with 0.1 gm. of the drug thrice daily for seven days the results were less satisfactory as the clinical attack was in some cases not arrested, while other patients experienced a rapid recrudescence of the attack. On this dosage there were no untoward symptoms caused by the drug.

V Further trials with 3349 given orally have now been carried out in 206 cases of benign tertian and in 61 cases of malignant tertian malaria under the same conditions as previously observed. Data have been collected on the relapse rates of patients treated with this drug. Details of the benign tertian cases are dealt with first. Many were treated for delayed primary attacks consequent on the discontinuation of prophylactic mepacrine. The effects of different dosage schedules of the drug on the temperature and on the number of asexual forms in the blood are recorded in a number of graphs. Retreatment of relapses was successful and provided no evidence of development of resistance to this drug. Sexual forms of the parasite were unaffected by 3349. The relapse rate in this form of malaria after effective clinical treatment was over 70 per cent in 126 cases within a period of eight weeks and was fairly constant in the different classes treated. In the case of malignant tertian malaria 15 acute attacks were treated with 0.1 gm. of 3349 thrice daily for seven days. As in benign tertian this dosage was unable to control all the attacks and asexual parasites were present in four of the cases on completion of treatment. Double this dose of drug was effective in 32 of 33 cases. Twenty seven of 28 attacks were successfully treated by 0.5 gm. of the drug given each twelve hours for 2-7 days. Good results were obtained in four patients treated with 1.0 gm. of drug on two occasions with a twelve hour interval between doses. Relapses were noted under all dosage schedules except in two cases when 1.0 gm. doses were given. The drug showed no activity against the crescent forms. Only the mild toxic symptoms due to the drug were encountered, as noted in the earlier studies and they did not prevent continuation of treatment. One patient after a dose of 1.0 gm. of the drug had severe diarrhoea.

VI When the action of 3349 was being tested on acute attacks of benign tertian malaria alternate and unselected cases were for a time treated with mepacrine hydrochloride. Both drugs were given orally and their administration was carefully supervised. Two hundred and thirty five cases were treated with 3349 in doses regarded as clinically effective as follows—

95 cases	0.2 gm. of 3349 thrice daily for 7 days.
28	0.5 gm. 3349 12-hourly for 2 days
54	0.5 gm. 3349
54	0.5 gm. 3349
4	1.0 gm. 3349
	4
	7
	1 day

For comparison 102 cases received 0.2 gm. mepacrine thrice daily for 2 days and then 0.1 gm. mepacrine thrice daily for 5 days—a dosage previously employed by the authors on an extensive scale in the control of all types of acute malaria infection. The experimental details for each drug are recorded in Figs. A and B in the paper. The following is the authors' comment—

A study of Figs. A and B shows very comparable activity of 3349 and of mepacrine hydrochloride in the arrest of acute attacks of *P. vivax* infection. In each series of cases gametocytes were observed to persist in the peripheral blood in about half the cases for periods up to a week after the end of treatment. In neither were the patients unduly inconvenienced by side-effects resulting from the treatment. The absence of yellow staining of the skin in those men treated with 3349 was held by them more than to counterbalance the mild colic or diarrhoea which some of them experienced for the first day or two of this treatment.

J. D. Fulton

SPINKS A. TOTTER Mary M. Studies on Synthetic Antimalarial Drugs.

VII. Turbidimetric Determination of 2- $\beta$ -Chlorophenylguanidino-4- $\beta$ -Diethylaminoethylamino-6-Methylpyrimidine (3349) [SPINKS]. *Ann. Trop. Med. & Parasit.* 1945 Dec. 31 v 39 No. 3/4 182-9 4 diagrams.

VIII. Colorimetric Determination of 2- $\beta$ -Chlorophenylguanidino-4- $\beta$ -Diethylaminoethylamino-6-Methylpyrimidine (3349) [SPINKS & TOTTER]. *Ibid.* 190-96 2 diagrams. IX. The Excretion of 2- $\beta$ -Chlorophenylguanidino-4- $\beta$ -Diethylaminoethylamino-6-Methylpyrimidine (3349) in Human Urine [SPINKS & TOTTER]. *Ibid.* 197-207 3 diagrams. [45 refs.]

VII. A turbidimetric method for the estimation of 3349 in biological material has been developed which is claimed to be simple and accurate. Reference is made to two other methods of estimation and also to a colorimetric method which is described in Part VIII of this series. The present method is accurate to within 10 per cent. and its sensitivity is given as about 2  $\mu$  gm. of 3349 in any biological material. It is founded on the fact that many basic substances form insoluble salts with complex acids. 3349 was found to give precipitates with a number of organic and inorganic acids and the potassium mercuri-iodide reagent of GRAYKOW [this *Bulletin* 1938 v 35 569] was found to be the most suitable in that the suspension formed was reasonably stable at high dilution. Precipitation of the base occurs in acid or alkaline solution with this reagent. It was brought about in N/10 hydrochloric acid since extraction was carried out with this reagent and results were best as regards opacity of the suspension with that particular concentration of acid. When formed, the suspensions were examined in a direct reading photoelectric colorimeter the percentage of light transmitted being in approximate agreement with the galvanometer deflections. The best results were obtained if galvanometer readings were made at 5-10 minutes after formation of the suspension and the temperature of the reaction or colour of the incident light did not affect the readings to any extent. To obtain the base from the purified biological material continuous extraction with ether was used and the solvent was completely removed before dissolving the base in N/10 HCl. The method can be applied to blood, urine and tissues of animals after administration of large doses of drug. It is not however suitable for human blood or plasma as the amounts of drug present in these substances are too small and the colorimetric method of estimation described in Part VIII is then recommended. In the preparation of a standard curve which could be maintained for permanent reference, the amount of 3349 base present in  $\mu$  gm. was plotted against deflections of the galvanometer. 2 ml. standards of the base in solution in N/10 HCl containing 0-50  $\mu$  gm. in each

different tubes were used in its construction and the contents mixed with 0.2 ml of mercuric iodide reagent. The deflections were read for each standard 5 minutes after mixing when the deflection of the blank had been made to read 100 on the galvanometer scale of the colorimeter. [The complete details of the method cannot be given here.]

VIII A colorimetric method more suitable for the estimation of 3349 in blood and plasma than the turbidimetric method outlined above is described. It depends on the hydrolysis of the substance to *p*-chloroaniline which is then diazotized and coupled with *N*- $\beta$ -sulphatoethyl-*m*-toluidine to give a red dye. As little as 0.4  $\mu$  gm of the drug is estimable in biological material. It was shown by large scale experiment that quantitative hydrolysis of 3349 by *N*/1 HCl to *p*-chloroaniline did not occur under normal pressure but was achieved by hydrolysis with *N*/2 HCl under a pressure of 20–25 lb for 12 hours. In the extraction previous to hydrolysis a mixture of benzene containing 2 per cent of ethanol gave 100 per cent recovery of 3349 from biological material by single extraction after the material had been basified and rendered less viscous by warming at 50°C for 30 minutes. All the reagents employed were of the highest purity. A standard reference curve was prepared in which  $\mu$  gm of 3349 per ml were plotted against drum readings of the Spekker absorptiometer and against galvanometer deflections in the case of the photo-electric colorimeter. In these determinations solutions containing 0.20  $\mu$  gm of 3349 per ml in *N*/2 HCl were hydrolysed in sealed ampoules under the conditions described above in volumes of 1–2 ml. On cooling 1 ml. aliquots were partially neutralized diazotized and coupled and after 10 minutes the yellow colour present was changed to red by 4 drops of concentrated HCl. The volumes were then corrected and readings made on the instrument selected, not more than 1 hour after coupling while using a filter with maximum transmission at 510  $m\mu$  since the absorption maximum of the coloured substance was at 507.5  $m\mu$ .

For estimation in the case of blood, 1–7.5 ml. are used and the blood is laked before being made alkaline. The next steps are as described above. The same principles are employed for estimation in the case of plasma, urine, bile, tissues and faeces. The four last may contain large amounts of drug. [Details are recorded in the paper but cannot be given here.] Mepacrine in high concentration may interfere with results and also phenacetin and procaine. Most tissues contain no reacting substances but blood may give a high blank. The recoveries of drug from blood, plasma, tissues, faeces and urine approached theoretical.

IX Using the turbidimetric method for the estimation of 3349 the authors measured its urinary excretion in four normal volunteers each of whom was given 500 mgm orally twice daily for 4–5 days. Nausea, epigastric pain and diarrhoea occurred and one subject vomited after the eighth dose. The urine of volunteers was collected regularly for 7 days previous to and for 14 days after treatment started, and irregularly till the amount of drug present was minute. While the drug was being taken there was a diminution in urinary output probably as the result of diarrhoea but there was neither glycosuria nor albuminuria. The percentage of the daily intake of drug excreted in the urine continued to increase while the doses were maintained but it was not constant by the fifth day when dosage ceased. After that time there was a rapid fall in output. Minute amounts of drug were still present in the urine 23 days after the start of treatment which suggested that it was being retained in the tissues. About 4 per cent. of the total drug administered was found in the urine of each volunteer and likewise in that of treated rabbits and rats in its manner of excretion 3349 therefore resembles mepacrine. Since it is shown in Part VII that *p*-chloroaniline was a hydrolytic product of 3349

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and possibly acetone as well, the excretion of aromatic amine of total amine, and of acetone was measured during the experiment. Paradoxically the amount of "total amine found was less than that of "free amine possibly due to the presence of esters of aminophenols. There was a significant increase in excretion of aromatic amine while the drug was being taken, but it represented only a very small conversion of 3349 to *p*-chloroaniline. There was no evidence that 3349 gave rise to acetone in the human subject. It is well known that many aromatic substances are converted in the body to hydroxyl derivatives which are then excreted as aryl sulphates or glucuronides. Measurements of the amount of detoxication of 3349 but none was obtained. A search for metabolites of 3349 was also made in urine but only the parent substance was isolated. By quantitative experiments in the isolation of added 3349 from urine it was shown that the substance estimated as 3349 by the turbidimetric method of Part VII was indeed that substance possibly contaminated with very small amounts of basic metabolites as judged by ultra violet absorption spectra. Work in progress suggests that most of the 98 per cent. of administered 3349 still unaccounted for may be present in faeces. The possibility of formation of a hydroxyl derivative of the parent substance the deamination of the latter or alteration in the side-chain is however not excluded.

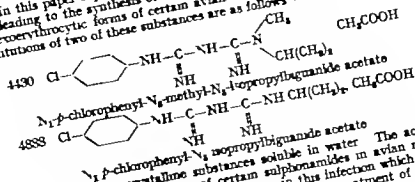
J D Fulton.

CURD F H S, DAVEY D G & ROSE F L. Studies on Synthetic Antimalarial Drugs X. Some Biguanide Derivatives as New Types of Antimalarial Substances with both Therapeutic and Causal Prophylactic Activity *Ann Trop Med & Parasit* 1945 Dec 31 v 39 Nos 3/4 208-18. [10 refs]

ADAMS A R D, TOWNSHEND R H & KING J D. XI. An Investigation of the Therapeutic Action of 4430 on Benign and Malignant Tertian Malaria. *Ibid.* 217-19

SPINKS A & TOTTER MARV M. XII. Determination of  $N_1$  *p*-Chlorophenyl- $N_2$ -Methyl- $N_3$ -Isopropylbiguanide (4430) and  $N_1$  *p*-Chlorophenyl- $N_2$ -Isopropylbiguanide (Paludrine) a Preliminary Report. *Ibid.* 220-24 1 diagram.

\. In this paper a preliminary account is given of the chemical considerations leading to the synthesis of biguanides with marked action on the blood and exoerythrocytic forms of certain avian malaria parasites. The chemical constitutions of two of these substances are as follows —



Both are colourless, crystalline substances soluble in water. The action of the former is analogous to that of certain sulphonamides in avian malaria, whereas the latter has some unique properties in this infection which suggest that an advance has been made in the prevention and treatment of malaria. While 4430 is a causal prophylactic against *P. gallinaceum* only and is ineffective against the blood forms of *P. cathemerium* 4888 acts both as causal

prophylactic and as a therapeutic agent in the four types of avian malaria studied. The probable life-cycle of the malaria parasite in the vertebrate host as outlined by a number of workers including HOFF *et al* [this *Bulletin* 1943 v 40 815 1945 v 42 538] and DAVEY [this *Bulletin* 1944 v 41 385] leads the authors to believe that drugs with an action against exo-erythrocytic forms are of paramount importance and that on this action causal prophylaxis and prevention of relapses probably depend. JAMES especially has long put forward similar views although the presence of such forms has not yet been satisfactorily demonstrated in human malaria. After the synthesis of certain pyrimidine derivatives described in Parts I and II of this series which contained an  $-NH-$  (imino group) or  $HN-C-NH$  (guanidino group) between the

$$\begin{array}{c} \text{NH} \\ \parallel \\ \text{HN}-C-NH \\ \parallel \quad \parallel \\ \text{NH} \quad \text{NH} \end{array}$$

ring systems theoretical considerations led the authors to the synthesis of compounds with a new linkage  $-HN-C-NH-C-NH-$  (biguanidino group). The

substitution of other heterocyclic ring-systems than pyrimidine opened further possibilities but the authors stress the practical need for simplicity of synthesis and the retention only of groups necessary for antimalarial activity. It was found that the pyrimidine ring was not essential. Biguanides are easily synthesized, and in this reaction ammonia or an amine takes part. The first member of the new series proved inactive in *P. gallinaceum* infection on account it was believed, of its too strongly basic character. By selecting suitable amines for the reaction the active substances 4430 and 4888 were obtained. [The latest views of the authors on these matters have recently been given to the Chemical Society.]

In the case of *P. gallinaceum* and *P. relictum* sporozoites have been shown to undergo a cycle of development in tissues and have been designated by the authors as primary exoerythrocytic (e.e.) forms. A causal prophylactic drug would act against either of these forms. No drugs are yet known which act against sporozoites but the properties especially of 4888 suggest that it may act as a causal prophylactic in human malaria. When the development of primary e.e. forms is completed the blood is then invaded and during multiplication in the latter site there is a concomitant increase in tissue forms. From the reaction of the tissue forms to drugs they appear to differ from primary e.e. forms they have been designated secondary e.e. forms and may be derived from blood forms as they can be transmitted by blood inoculation. Since a radical cure of avian malaria is not easily obtained in which respect it resembles benign tertian malaria the presence of secondary e.e. forms in the latter infection although not yet demonstrated may be the explanation of the failure to effect cure. The search for a drug active against the blood forms of human malaria but without the practical drawbacks of mepacrine both as regards dyeing properties and the many steps in its synthesis has not been neglected. A comparison of the action of 4430 and 4888 as causal prophylactics and in treatment of blood infections has been made with that of quinine mepacrine and sulphonamides in four species of avian malaria and the results are given in a table. The properties of the two new drugs were such as to justify their trial in human malaria.

XI This note records the first trials in human malaria of the new drug 4430 described in Part X. The early dosages ranged from 20-500 mgm. orally thrice daily without evidence of serious effects. When 1 gm doses were given more or less severe toxic symptoms were encountered. Benign and malignant tertian malaria naturally acquired was treated in healthy subjects after their return from service overseas. Most of them had taken mepacrine

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or quinine prophylactically and there was in some cases a history of previous chemical attacks. The conditions of treatment were the same as those described in Part III and subsequent papers of this series. In 44 cases of benign tertian malaria the clinical attack was rapidly cured within 72 hours and the peripheral blood was freed from parasites within 96 hours after the start of treatment but gametocytes were present after 6 days. The details of these cases are recorded in tabular form. More than half the cases relapsed independently of the dosage given. In nine cases of naturally acquired *P. falciparum* infection similar results were obtained. The crescent forms appeared to be unaffected by the drug but in two receiving the highest dosage given for 1 week, no relapse occurred. Doses of 1 gm. or more of the drug daily caused nausea and vomiting. The highest doses gave rise to loss-pains, vomiting, sweating, *urticaria*, albuminuria and haematuria or the presence of red cells in the urine. With copious fluids, recovery was complete in 24 hours. In subsequent cases a liberal fluid intake when the drug was being administered avoided renal complications.

XII. This is a preliminary report on the estimation of the two drugs 4430 and 4888 (Paludrine) described in Part I of this series. On account of the presence of a  $\beta$ -chlorophenylguanidine residue which can be hydrolysed to  $\beta$ -chloroaniline apparently more readily than in 3349 the same colorimetric method of estimation can be employed as for the latter substance. The two newer drugs are recoverable quantitatively from blood, plasma, and tissues with the same method of extraction. In their case  $\frac{1}{4}$  HCl is used for both extraction and hydrolysis and partial neutralization becomes unnecessary. Details of the method are given for blood, and it can be adapted to other biological materials. As before, it consists essentially in taking, basifying, rendering less viscous by heat, and then extracting the base with benzene-ethanol. An aliquot is then hydrolysed under pressure in a sealed subs-stance which is estimated in a photoelectric colorimeter not more than one hour later and compared with a standard curve compiled from known amounts of material. On account of lower molecular weights of 4430 and 4888 smaller amounts can be estimated than in the case of 3349 and the levels of the former are actually higher in blood, plasma and urine but not in faeces and tissues. The amounts estimable depend on the apparatus available. Some instru-ments allow 0.2  $\mu$  gm. in aqueous solution to be estimated, but the sensitivity of the method can be increased 3-5 times by special apparatus. Purity of reagents and cleanliness of apparatus are vital for success with these small amounts, and frequent blank determinations should be used as check. Recovery from plasma and urine approached the theoretical while the accuracy was somewhat lower in the case of blood and tissues.

J. D. FALLON

- ADAMS, A. R. D. & MARGRAITH, B. G., KING, J. D. & TOWNSHEND, R. H., DAVEY, T. H. & HAYWARD, R. E. Studies on Synthetic Antimalarial Drugs. XIII. Results of a Preliminary Investigation of Benign Tertian Malaria. *Ann. Trop. Med. & Parasit.* 1945 Dec 31 v. 39 Nos. 3/4 295-314 figs.
- MARGRAITH, B. G., ADAMS, A. R. D., KING, J. D., TOWNSHEND, R. H., DAVEY, T. H. & HAYWARD, R. E. XIV. Results of a Preliminary Investigation of the Therapeutic Action of 4888 (Paludrine) on Acute Attacks of Malignant Tertian Malaria. *Ibid.* 1945 Dec 31 v. 39 Nos. 3/4 315-328 figs.
- XV. This preliminary report describes the first clinical trials with "Paludrine" (4888) given orally in acute attacks of benign tertian malaria. The

tests were initiated when it was found that the drug was probably curative in *P. gallinaceus* infections of chickens. The patients were Service men suffering from primary attacks of benign tertian malaria or from relapses. No patient in whom the clinical attack had lasted more than one week was included in the series. Suppressive mepacrine had been taken by most and some had been treated with the standard antimalarials in all cases more than two weeks before hospitalization. The same conditions of treatment were observed as described in Part III etc. of this series. Experimental data in animals suggested that 40 mgm per day would be a safe dose in man and 20 mgm were therefore given 12 hourly on 14 consecutive days a treatment which proved clinically effective. The dosage was increased step-wise to 700 mgm. twelve hourly in later cases and careful watch was kept on the patients for any untoward symptoms. Doses of 10 mgm. 12-hourly were successfully employed in three cases but below this level clinical results were variable. Blood films were examined twice daily till parasites disappeared, and thereafter daily while the patient was under observation. The detailed results of treatment of 147 cases with doses ranging from 10 to 700 mgm. 12 hourly for 14 or 28 days are recorded graphically along with those for 183 similar cases treated with mepacrine in doses of 0.8 gm. daily for two days followed by 0.3 gm. daily for 10 days. Paludrine controlled the acute attacks over the range studied as effectively as mepacrine. Toxic symptoms seen in a few cases included vomiting and epigastric pain but it was never found necessary to interrupt treatment and regular urine examinations disclosed no abnormality. Estimations of drug concentration in whole blood, plasma and urine have been made following single doses of 50 and 500 mgm. In whole blood the estimations were unreliable as previously observed for mepacrine and were therefore abandoned. The plasma and urinary concentrations after the standard therapeutic dosage with 50 or 500 mgm. 12-hourly for 14 days were also determined. In these cases the plasma concentration rose rapidly and remained fairly steady from the fourth to fifth day of treatment. When treatment ended there was a rapid fall in the concentration. The urinary output followed a similar pattern and in urine the drug was detectable in some cases for nine days after the end of treatment. The fall in plasma level and in urinary output are more rapid than in the case of mepacrine.

XIV The treatment of 22 cases of recently acquired malignant tertian malaria with Paludrine (4888) orally is reported in this note. Sixteen of the patients had no previous history of malaria the others had had one previous attack of malignant tertian malaria. Seven had received no suppressive treatment while the remainder had taken quinine or mepacrine. No anti-malarial treatment had been given for at least two weeks before treatment with Paludrine was begun. All the subjects were kept in bed and the conditions of treatment as outlined in Part III were observed, except that in some cases the patients were ill on admission and treatment was started within 24 hours. The first dosage schedule tried was 50 mgm. 12 hourly for 14 days and during treatment the patient was encouraged to drink plenty of fluids. The clinical attack was controlled in all cases with the above dosage. Later cases were given 200 500 or 600 mgm doses in the same way. Therapeutic results were judged as in previous trials. With this treatment asexual parasites rapidly disappeared from the peripheral blood temperature was controlled and the condition of the patient rapidly improved. Gametocytes were unaffected. The clinical results obtained so far are comparable with those in benign tertian malaria. A few patients vomited after the drug but probably not on account of it as vomiting ceased with improvement of the clinical condition. There were no other untoward effects.

J D Fulton



KELSEY F. E., OLDFHAM F. K. & CCELLIX E. M. K. Studies on Antimalarial Drugs. The Metabolism of Quinine and Quindine in Birds and Mammals. *J Pharm & Exper Therap* 1945 Oct. v 85 No 2, 170-75 1 fig

In previous papers Kelsey and Oldham [this Bulletin 1944 v 41 260] have investigated the ability of tissues of different species of animals to metabolize quinine *in vitro* and have suggested that there is a probable relationship between *in vitro* and *in vivo* metabolism. In a similar way *in vitro* studies have now been made on the metabolism of quindine—the optical isomer of quinine—by tissues of various birds, rats and rabbits. Tissues were homogenized in a Waring Blender in Ringer Locke solution and filtered through gauze. Aliquots representing different weights of tissue were mixed with 0.1 mgm. of the two alkaloids in 10 cc. Ringer-Loeke solution which was used to make the total volume up to 20 cc. After incubation for 6 hours at 38–40°C. the percentage degradation of these substances was estimated by a method previously employed by the authors. In the *in vivo* studies adult rabbits, chickens and ducks were given 10 mgm. of the alkaloids per kilogram intravenously and were sacrificed 10 minutes, 1 hour and 4 hours after injection of the drug. Post-mortem degradation in the weighed tissues was prevented by 2 per cent. NaOH. *In vitro* it was found that quinine was more readily metabolized than quindine by rat and rabbit tissues, while the converse was true when tissues from various birds were used. The rabbit metabolized quinine more rapidly than quindine *in vitro* whereas in the duck and chicken both appeared to be metabolized at similar rates, the rate in the duck being slower than in the chicken. Papers by KELSEY *et al* [this Bulletin 1944 v 41 11], WALEZKY & BROWN [ibid. 1944 v 41 183] and by HIAATT & QUINN [ibid. 1945 v 42, 773] are of interest in this connection. The distribution of these alkaloids between red cells and plasma in the case of ducks and chickens was found to be different. These experiments show that the fate of the two drugs in the chicken and duck is not identical and the results of antimalarial tests in the two species may thus be different.

J. D. Fulton

DEARBORN E. H. & MARSHALL, E. K. Jr. The Degradation of Quinine in the Duck, Chicken and Dog. *J Pharm. & Exper Therap* 1945 Oct., v 83 No. 2, 202-5. 12 refs.]

Different methods for the estimation of quinine in the blood and tissues of animals have been described [this Bulletin 1944 v 41 11 188 260 1945 v 42, 778]. In some of these cases the method of assay has included degradation products of the alkaloid. In the present investigation quinine was administered to ducks and chicks by the drug-diet method of MARSHALL *et al* [this Bulletin 1943 v 40 223] or intravenously and by the latter method to dogs. By the use of selected methods devised by BROWN and UDENFRIEND for the estimation, the evidence obtained suggests that more than one degradation product of the alkaloid was formed. By the first method [this Bulletin 1943 v 40 821] total acid-soluble fluorescence is estimated by the second, fluorescence after alkaline extraction and in the third, which proved most reliable for the estimation in plasma, the base is made to combine with methyl orange after alkaline extraction (*J Biol Chem* 1945 v 158 705). The quenching of fluorescence by salt in the first method suggested that only traces of the degradation product described by KELSEY *et al* [this Bulletin 1944 v 41 923] were present, and this was supported by other evidence. The concentration of "quinine" in the plasma of ducks, chicks and dogs was estimated by each method, and also that in the liver of chicks and ducks. By the use of what was termed "quinine oxidase" of rabbit liver by KELSEY and OLDFHAM [this

*Bulletin* 1944 v 41 260] which converts quinine to a 2-hydroxy derivative as shown by MEAD and KOEFFLI [this *Bulletin* 1945 v 42 9] successful degradation of quinine was accomplished in duck plasma, but only to a limited extent in plasma of chicks or dogs.

From the results obtained by the three different methods of estimating quinine the authors conclude that —

- (1) There are probably at least two degradation products of quinine to be found in the duck after administration of quinine.
- (2) The degradation of quinine appears to be qualitatively similar in ducks, chicks and dogs.

MERGEVER, J. C. *Psychosis following Administration of Quinaerine Hydrochloride for Malaria. Neuropsychiatric Study of a Case* *War Medicine* Chicago 1945 Oct v 8 No 4 250-52. J. D. Fulton

A soldier 25 years of age suffered from a primary *P. falciparum* infection and was treated with quinaerine (mepacrine). During a period of five days he received 2.8 gm. On the fifth day signs of mild excitement appeared: he became very talkative, his speech was rambling and at times disconnected and it was impossible to keep him in bed. A sedative was given, quinaerine was stopped. The excitement increased the next day, euphoria and hyperactivity necessitated his being placed in a locked ward. The hyperactivity gradually gave way to a confusional state which bordered on depression; he became disoriented for time, place and person. His replies to questions became slow and reflected inner confusion. A possibility that cerebral malaria might be the cause of the psychosis prompted the administration of quinine. For six days his condition changed but little, then gradual improvement began. In all the mental disturbances lasted 14 days before recovery was complete. When he was discharged from hospital a fine tremor of the hands persisted. Several interviews after his recovery failed to reveal anything psychiatrically abnormal and there was no antecedent history of psychiatric factors which might have predisposed to the onset of mental symptoms. No recurrence of the symptoms had been noted three months after recovery. [See also this *Bulletin* 1945 v 42 9 1946 v 43 297] Norman White

ZYLMAN, G. *In vitro*—und *in vivo*—Versuche über die hämolytischen Eigenschaften der synthetischen Malariazmittel. [*In vitro* and *in vivo* Experiments on the Haemolytic Properties of Synthetic Remedies for Malaria.] *Deut. Tropenmed. Ztschr.* 1944 Jan. 1 v 48 Nos 1/2 7-18 [15 refs.]

This paper contains a brief review of the German literature on the subject. The *in vitro* experiments were designed to compare the lytic action in human cells (from normal persons and patients with MT and BT malaria) of equivalent serially diluted solutions of quinine, atabrin, plasmoquine and a Priparat x.

Quinine had a lytic effect on all red cells over a range of concentration of 1/50 to 1/800 molar. Atabrin lysed normal red cells over a range of concentration of 1/50 to 1/200 molar; it lysed cells from both BT and MT patients at dilutions of up to 1/400 molar. The author concludes that the haemolytic effect of atabrin is more pronounced on cells from malaria patients than on those from normal subjects. (Three normal persons, three MT cases and eleven BT cases were examined.) Plasmoquine had little effect except for a very slight lytic action in the middle range of concentrations. Priparat x had no lytic action. The author attempted to repeat with atabrin KOCIR and KIKUTH's experiments with quinine [this *Bulletin* 1929 v 26 1028]. Atabrin by itself had

no lytic effect. amboceptor gave rise to haemoglobinaemia in one animal, and haemoglobinuria in two (out of four). Amboceptor and atabrin injected together gave rise to haemoglobinaemia in three, and haemoglobinuria in two animals (out of four). The author considers that this results indicate that atabrin has a strengthening effect on the haemolytic action of the amboceptor. He points out that more *in vivo* experiments are required to substantiate this. [No account of the composition of Präparat X is given, presumably because the paper was published during the war.]

B G Margnath

MOHR, W. Atebrin-Leberempfindlichkeit. [Hypersensitivity to Atabrin.] *Deut. Tropenmed. Ztschr.* 1944 Apr-May v 43 Nos. 7/10 177-82.

The author reviews the available literature on atabrin sensitivity and notes that with the usual dosage régimes, evidence of true sensitivity is very rare. Atabrin poisoning is not common even after high dosages. In the literature reviewed, which includes an account of malaria in German troops in the recent war, only three cases of idiosyncratic allergic reactions to atabrin are described.

The author describes a case in which the patient developed a resistant urticaria after atabrin administration for the treatment of malaria (species of parasite not determined, but thought to be *Plasmodium falciparum*). Skin tests showed this patient to be sensitive to atabrin, but not specifically he was also sensitive to quinine (to a lesser degree) and to a variety of food substances including meat and mushrooms.

B G Margnath.

YUDEN, J. Non-Absorption of Mepacrine. Description of a Case. *Brit. Med. J.* 1946 Feb. 23 271. 1 chart.

A case of M.T. malaria in a European in West Africa which failed to respond to intensive therapy with oral mepacrine is described. Urinary analysis showed that the patient was not absorbing the drug. Subsequent administration of mepacrine intramuscularly resulted in a rapid recovery.

BREBLOW, D. S. WALKER, H. G. YOST, R. S. SEEVERS, J. C. & HACKER, C. R. Synthesis of Antimalarials. IV. The Synthesis of certain Compounds related to Quinaerine. *J. Amer. Chem. Soc.* 1946, Jan., v 68 No 1 100-102. [Refs. in footnotes]

BERCOVITZ, Z. T. Malaria complicated by Pneumonia. Treatment with Sulphadiazine and Atabrine. *Ann. Intern. Med.* 1945 July v 23 No 1 79-82.

This is a case report of a patient who suffered concurrently from *P. falciparum* malaria and lobar pneumonia, type 7 pneumococcus. The administration of atabrine did not in any way influence the effect of sulphadiazine on the pneumonia. The patient received 59.5 gm. of sulphadiazine over a period of 12 days. Atabrine 0.1 gm. daily was given for 22 days while he was under treatment for pneumonia, and for 60 days on two occasions subsequently without harmful effect. Reference is also made to another similar case in which atabrine and sulphathiazole were used with success. Norman White

COXON, R. V. & HAYES, W. Investigation into the Efficacy of Sulphadiazine in the Treatment of Malaria. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945 Dec. v 39 No 3 195-205 2 graphs.

Twenty cases of malaria, including fresh and relapsing cases of benign tertian and of malignant tertian, and one quartan infection were treated with

sulphadiazine. Ten cases receiving only non-specific symptomatic treatment served as controls. Comparison was also made with results achieved by quinine-atebrin plasmoquine treatment. The dosage of sulphadiazine in most cases was a loading dose of 5 gm. in the first 4 hours followed by 1 gm. 4-hourly [apparently for 12 days]. With this dosage the concentration in the blood remained at approximately 10 mgm per 100 cc. throughout the course.

For the enumeration of parasites an absolute method of counting was used: oxalated blood was drawn up to the 20 cmm. mark of a Sahli haemoglobinometer pipette and then discharged on a slide and spread accurately and evenly over an area of 2 sq cm. The film was allowed to dry on a level surface and dehaemoglobinized with distilled water and stained by Field's stain. Before a sample of blood was reported negative at least 100 fields representing 0.5 cmm. blood were examined. The advantage of this thick film method over the thin was shown in the first twelve cases treated with sulphadiazine: the average day after the beginning of treatment on which the blood first failed to show parasites was 3.7 by the thin and 8 days by the thick film method. The average duration of fever after commencement of treatment with sulphadiazine was 4½ days in *P. vivax* infections, 6 days in *P. falciparum* infections. Of the untreated controls four spontaneously lost their fever within 12 days of onset in the remaining six the fever was virtually unaltered in degree at the conclusion of the 12th day.

The average time for the blood to become parasite free (asexual forms) after the beginning of treatment was 8 days for both *P. vivax* and *P. falciparum* infections. This does not refer to gametocytes. None of the untreated controls was free from parasites within the 12-day period of observation. In nearly all sulphadiazine treated patients the parasite count began to fall soon after the commencement of treatment and steadily declined to zero. In only one case did the parasites appear to be resistant to the drug. With quinine there was a complete clearing of the blood within 5 days. Gametocytes appeared to be completely unaffected by sulphadiazine. Several patients were given higher doses than the standard 15 gm a maintenance dose of 2 gm. 4 hourly thus securing blood levels of 17-20 mgm per 100 cc. The response was not materially different from that obtained by the standard dose.

Of the 20 cases treated with sulphadiazine 15 relapsed within one month from the end of treatment. Fifteen cases that had received standard army treatment—quinine 4 gm. atebriin 1.5 gm. and plasmoquine 0.15 gm over a period of 14 days—only one relapsed during a period of one month.

The only complications of treatment apart from vomiting in a few patients were renal. Four patients had renal colic, two of these had haematuria but no crystals of the drug were found in the urine. In no case was there a dangerously low white blood cell count. Sulphadiazine has definite antimalarial properties but the action is inferior and slower than that of either quinine or atebriin and treatment with it is followed by a much higher relapse rate. The inquiry revealed that the corrected erythrocyte sedimentation rate is no value in assessing the probability of relapse after treatment in malaria.

Norman White

ENSON D S The Use of Calcium Gluconate in the Treatment of Malarial Chills. Puerto Rico J Pub Health & Trop Med 1944 June v 19 No 4 602-13 2 figs [20 refs] [Spanish version 614-25]

most distressing symptom of malaria is the chill that usually precedes fever. These chills may last from a few minutes to over three hours. The reports the results of treatment of malarial chills.

As soon as possible after onset of the chill, 10 cc. of a 10 per cent. solution of calcium gluconate is given intravenously very slowly. Fifty trials were carried out on 40 patients and the results are tabulated. In only 2 trials did calcium fail to have an observable effect, and in both these the chill had lasted some time before treatment was given. All cases treated within 5 minutes of the onset of the chill showed complete relief within an average time of 3.7 minutes after injection. If the injection was delayed more than 5 minutes after the onset of the chill the chill had an average duration of 9.7 minutes. In some cases relief is almost instantaneous. Most of the cases treated were *P. vivax* infections; there were however 5 *P. falciparum* and 4 mixed infections. All responded equally well.

In the 50 trials 14 patients complained of untoward effects: nausea and vomiting 4, headache 6, oppression over the chest 1, epigastric discomfort 1, flushing of the face 1, dizziness 1. None of these symptoms was severe enough to suggest that calcium gluconate should not have been given.

The precautions recommended are: careful venipuncture to avoid extravasation of calcium solution into subcutaneous tissue, which might cause necrosis; slow injection; the patient should be recumbent for 15 minutes after the injection. Intravenous calcium is contraindicated in cardiac cases, particularly those with arrhythmias and bradycardia and in patients receiving digitalis therapy.

Norman White

MORRIS, W. Zur Behandlung der Malaria tertiana mit intravenösen Gaben von *Tartarus stibiatus*. [The Treatment of Benign Tertian Malaria by Intravenous Doses of Antimony Tartrate.] *Deut. Tropenmed. Ztschr.* 1944 Apr-May v. 48 Nos. 7/10 169-76 2 figs. (18 refs.)

The author reports the use of intravenous antimony tartrate in four cases of inoculated benign tertian malaria. This treatment has no advantage over atabrin in the acute malarial attack but may be indicated in relapses occurring very soon after curative treatment. Combined therapy may assist erythropoiesis. The X-ray shadows of both spleen and liver are intensified under antimony treatment.

B. G. Macgregor.

BRATTON, A. C., Jr. A Short-Term Chronic Toxicity Test employing Mice. *J. Pharm. & Exper. Therap.* 1945 Oct. v. 85 No. 2, 111-18, 3 figs.

In the preliminary testing of antimalarials it was necessary to carry out chronic toxicity determinations on the more active new substances. For this purpose the drugs were incorporated in the diet of mice and to meet possible criticisms of this method it was shown by experiment that the results differed in no essential respects from those obtained through giving the drugs by stomach tube. The mouse has certain advantages over the rat as an experimental animal, in that drug-diets can be quantitatively administered, less drug is required per animal, and the intake of the mouse is, in general, more satisfactory. In this communication, the method of administering drug-diets to groups of 10 mice for a period of 7 days is described. Valuable information was obtained by this means regarding the toxicity of these substances in man. A simple type of cage with feeding arrangements was used, in which each animal was housed individually. Sufficient diet was prepared for each group of mice using starch as excipient for the drug before incorporation with the main diet in different concentrations. Mice weighing around 16 gm. were found most satisfactory

and in practice the total weight of a group was used for assessment of results. The animals not excessively hungry when the experiment started, were kept on a schedule of light and dark, 3 hours of each alternately, and the drug was therefore administered in a manner resembling that employed in human malaria where several daily doses are usually given. The amount of diet consumed, day of death and other relevant data were recorded. Many factors had to be considered in interpreting the results. Death of the animal proved the most reliable guide in evaluating the toxicity of large numbers of compounds. The mean daily drug intake which allowed the survival of 9 out of 10 mice over the experimental period was selected as the objective. Many data were collected on weight loss under different régimes of diet and they generally indicated a different value for toxicity from that based on death as the end point. In each experiment a suitable compound was chosen as a reference standard for toxicity. The value of the method may be judged by the fact that quinaquine [mepacrine] hydrochloride was found to be four times as toxic and pamaquin hydriodide 14 times as toxic as quinine hydrochloride.

J D Fulton

RIBBANDS C R The Use of DDT as a Mosquito Larvicide on Still Waters  
Bull Entom Res 1945 Nov 36 Pt. 3 315-30

The effect of DDT both in oil solution and as a dust was tried in a number of artificial breeding pits 4 ft x 3 ft. filled naturally with seepage water and containing larvae of *Anopheles culicifacies*, *A. vagus*, *A. barbirostris* with a few *A. hyrcanus* and *A. subpictus*. Preliminary control trials showed that oil itself at a dose of 4 pmts per acre had no deleterious effect on larvae and twice this amount produced a reduction which was not necessarily significant. Five per cent DDT in oil at doses of one third and one-half pint per acre caused 90 per cent mortality of anopheline larvae and doses over one pint consistently caused 100 per cent mortality in 24 hours. Malariaol kerosene and waste engine oil were used as solvents and it was found that the vehicle made no appreciable difference to the efficiency of the DDT. It does not kill eggs hence young larvae may hatch out soon after treatment with heavy doses, a fact which may obscure the residual action if all larvae are counted a better guide to effectiveness being the presence of 2nd to 4th instar larvae. Using this as a criterion doses of 2 gallons of 5 per cent solution per acre give complete control for 11 days 30 per cent control up to the 18th day and some degree of control up to a month whereas oil itself is completely ineffective by the eleventh day.

A series of trials was made in natural waters with the object of determining the average distance through which small quantities of DDT in waste engine oil would spread and exert a lethal effect when applied at a single point. Small quantities of oil solutions were applied by means of a pipette at the edge of breeding places and the extent of the perimeter sterilized of larvae was measured. Some of the results being summarized below.

From these results it is concluded that DDT solutions are lethal in the field and far reaching monomolecular films which are the final end of all oil solutions on a water surface. The application of these conclusions was checked by controlling breeding in a marsh by the distribution of DDT oil solution cast on in 5 cc. doses at intervals of 12 ft around the perimeter. The use of very simple apparatus is recommended. [These observations on the spread of DDT solutions are of considerable practical value for they indicate that there is no need for spraying apparatus more complicated than an oil-can or a drop bottle. It is unfortunate that the use of a trade-name the R.W. oil squirt, tends complication to a paper which otherwise goes far to simplify technique.]

TABLE X.  
Distance of Complete Anopheline Kill

Expt.	Type of Pond	Weather	Distance of Complete Anopheline Kill, in feet				
			$\frac{1}{2}$ cc	1 cc	2 cc.	4 cc.	8 cc.
1	Open Water	3 hours Rain	—	10	23	—	40
2	Weedy Pond	2 $\frac{1}{2}$ "	15	—	—	—	—
2	"	"	7	7	—	29	63
3	"	Fine	—	28	—	59	—
4	"	"	—	41	65	70	100
4	"	$\frac{1}{2}$ hour Heavy and 2 hours Light Rain	—	32	40	67	67
5	Pistia covered Pond	Fine	12	7	—	25	—
5	"	2 $\frac{1}{2}$ hours Rain	15	10	—	27	—
5	"	"	—	10	—	—	—
5	"	2 "	13.4	20	—	29	—
5	"	" "	—	20	—	—	—
Minimum Length of Kill			7	7	23	25	40
Average Length of kill			12	19	42	44	67

G Macdonald

DEONIER, C. C & BURRELL, R. W. Airplane Application of DDT Larvicides.  
*J Econom Entom* 1945 Aug v 38 No. 4 425-7

The application of DDT as a dust from aircraft presents several technical difficulties and is not a certain means of killing mosquito larvae. The application of solutions or emulsions by this means however is a very promising method of mosquito control. Less weight of material need be carried than when Paris green is being applied, the droplet size can be regulated, low flying is not necessary and the method is convenient. Preliminary tests gave kills varying from 94.9 per cent. to 100 per cent. in vegetated marshes and 100 per cent. in open water. Further studies are in progress.

G Macdonald

HAWKING F. Growth of Protozoa in Tissue Culture. I. *Plasmodium gallinaceum* Exoerythrocytic Forms. *Trans Roy Soc. Trop Med & Hyg* 1945 Dec., v 39 No. 3 245-63 29 figs. [12 refs.]

The paper describes the author's attempts to cultivate *Plasmodium gallinaceum* *in vitro*. He had little success with the erythrocytic stages. The utmost was a survival of parasites for five days as proved by injection of clean chicks. The inoculation of chick embryos was carried out by various methods on 69 eggs. In most cases the embryos died, but on 14 occasions chicks hatched. In no case were malarial parasites present in the blood at the time of hatching but in three they appeared in 10 to 14 days. As noted by the author in his preliminary paper [this *Bulletin* 1944 v 41 732] striking results were obtained with exoerythrocytic stages grown in cultures of macrophages and related cells. The tissue cultures were set up in Carrel flasks to the bottom of which four to six cover glasses were fixed by means of fowl plasma. On each cover glass a drop of plasma is placed and a small portion of the tissue to be cultivated usually the spleen is introduced into this plasma by means of a pipette which also serves

for the removal of excess of plasma. When the plasma has coagulated and the embedded tissue is fixed to the cover glass the fluid medium (Tyrode's solution) is added. The cultures are incubated at 37°C.

When the cultures were started from the tissues of chicks previously inoculated with sporozoites of *P. gallinaceum* developmental forms of this parasite appeared in the macrophages and other cells. These were detected by removing one of the cover glasses and examining it microscopically after fixing and staining the growing cells and parasites on its surface. Positive cultures have been obtained from the spleen bone marrow buffy coat of centrifuged blood and liver. In spite of its heavy content of exoerythrocytic forms the brain failed to yield a positive culture. In any positive culture parasites in all stages of development are present at the same time—forms with one, two, four and more nuclei (up to 50 or more) within the cytoplasm of the cells. Extracellularly sporozoites may be detected. These have a central nucleus and are rounded at one end and pointed at the other. Toward the rounded end a granule of volutin is often present. Usually the cultures were made from the tissues of the chicks or 8 days after the inoculation of sporozoites. Positive cultures have however been made before this the earliest being one hour after the inoculation of sporozoites. In some instances tissue cultures started from the spleen of an uninfected chick have been infected by introducing parasites from a positive culture but attempts at further passage were not successful. The viability of the parasites in cultures was tested by inoculation of chicks. The oldest culture which proved infective was one at its 89th day. Microscopically parasites were detected in cultures up to 61 days but with increasing age more degenerating cells and parasites occur. Attempts to commence cultures by introducing sporozoites into tissue cultures were not successful nor was it possible to infect erythrocytes by introducing these to cultures. In general the development of *P. gallinaceum* in cultures corresponds very closely with the course of development of the parasite in chicks following sporozoite inoculation. The paper is illustrated by photomicrographs and by a series of black and white drawings of the various stages described.

C. M. Wenyon

BRACKETT S. WALETZKI E. & BAKER Margaret. The Rate of Action of Sulfadiazine and Quinine on the Malarial Parasite *Plasmodium gallinaceum*. *J. Pharm. & Exper. Therap.* 1945 July v 84 No 3 254-61 2 figs [13 refs.]

It is agreed that sulphonamides generally exert their full inhibitory effect on bacteria only after a time lag and similar observations have been made in regard to malarial parasites. The authors suggest that in general the rate of action of these drugs may vary inversely with the rate of growth and reproduction of the organism in question. They have tested their view in the case of the relatively slow growing protozoan *P. gallinaceum* by comparing the results of treatment of this infection in chickens with quinine which acts quickly with those following treatment with sulphadiazine or a derivative. Two experiments with similar results were made in which 15 one week-old chicks were inoculated intravenously with a homogeneous suspension of small forms of the parasite from a donor bird, two days after drug administration had begun. Five of the chickens received a diet containing 0.2 per cent. of sulphadiazine five others received quinine in similar amount and the remaining five served as controls. The resulting blood level of sulphadiazine was well above that giving maximum activity in this infection. The course of the infection was followed by making parasite counts immediately after inoculation and 12 hourly thereafter. Differential counts of the parasites were also made in four groups according to size as a guide to the effect of each drug on growth and reproduction. It was



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found that sulphadiazine inhibited growth only after 24 hours, whereas the effect of quinine was very rapid. Treatment of the first generation with the former drug caused a reduction in the number of merozoites but segmentation was completed and new red cells were invaded without the succeeding development going beyond the four-nucleate stage. The maximum number of parasites was present on the second day of treatment and then gradually declined, whereas in the case of quinine there was no increase of the original numbers. Morphological changes in the parasites occurred more quickly with quinine than with sulphadiazine. In a further experiment with sulphadiazine and its bromo-derivative action against erythrocytic and exoerythrocytic forms in sporozoite-induced infections was also slow.

The view of the authors that the time required to cause effective inhibition by slow-acting drugs like the sulphonamides, increases in proportion with the slowness of the rate of growth of the organism, appears to be confirmed, and may be of practical significance in chemotherapy.

J. D. Fulton.

ZUCKERMAN, A. In Vitro Tests with *Plasmodium gallinaceum* and *Plasmodium lophurae*. *J. Infect. Dis.* 1945 July Aug. v 77 No. 1 28-39 4 graphs & 1 pl. 36 refs.

Having devised a technique for growing macrophages *in vitro* from the blood agranulocytes of chickens, their phagocytic powers against pneumococci in the presence or absence of antipneumococcus opsonic serum was tested. It was found that many pneumococci were phagocytized by the macrophages in the presence of 1:1000 diluted serum, but that phagocytosis was negligible in the absence of immune serum. In addition to being phagocytized, the pneumococci were agglutinated and became adherent to the macrophages. Having demonstrated that opsonization occurred in the case of bacteria, the test was applied to malarial parasites (*P. gallinaceum* and *P. lophurae*) in chickens. It was found that phagocytosis of infected red cells occurred in the presence of hyperimmune homologous serum, but not in the presence of normal chicken serum or of serum from chickens which had merely recovered from an acute initial infection. In addition, as in the case of the bacteria, there was agglutination of the infected cells and their adhesion to the macrophages and to the surface of the glass. These various phenomena involved not only infected cells but also uninfected cells, and any free parasites which were present. It was found that the antibody responsible for stimulating phagocytosis in the case of *P. gallinaceum* was more readily absorbed by the parasitized red blood corpuscles, an observation which suggests that the absorbing material is a constituent of the normal red blood corpuscles. There was some evidence that opsonization occurred not only *in vitro* but also *in vivo* for the phagocytic index in the presence of normal serum was higher when the parasitized red cells were collected at the time of the crisis than when they were collected before or after this event. This is a long paper describing in detail the method of cultivating the macrophages and the various procedures which have to be carried out in order to obtain the data for calculation of the opsonic indices. The appearances of phagocytosis and adhesion are illustrated in a plate of 13 figures.

C. M. Wenyaw.

SEILER, A. O. & OTT, W. H. Studies on Nutrition and Avian Malaria. III.—Deficiency of "Folic Acid" and other Unidentified Factors. *J. Infect. Dis.* 1945 July-Aug., v 77 No. 1 82-4

It is shown that *P. lophurae* infections, as judged by parasite counts are more severe in chicks on a diet deficient in "folic" acid and other unidentified

factors than in those on an adequate diet. The chicks on the adequate diet weighed 150 gm. at three weeks whereas those on the deficient diet weighed only 100 gm. The continued passage of the strain of parasite through chicks on the deficient diet did not lead to any enhanced virulence for whenever the strain was inoculated to chicks on adequate diet it behaved as did the control strain kept in serial passages in chicks on adequate diet. It seems evident that the severity of the infection is directly related to the nutrition of the host.

C M Wemyss

BRATTON A C Jr Continuous Intravenous Chemotherapy of *Plasmodium lophurae* Infection in Ducks. *J Pharm & Exper Therap* 1945 Oct. v 85 No 2 103-10 1 fig

A method has been devised to avoid the difficulties which occur owing to incomplete absorption and possible degradation of drugs in the alimentary canal of ducks when assessing the value of antimalarials administered to them by mouth. It consists in giving a continuous intravenous infusion of a solution of the substance under test over a period of three days. By this means precision in dosage can be attained and a new method of studying certain problems in chemotherapy is made available. White Pekin ducks infected with *P. lophurae* were used. In order to limit loss of body weight during the test an average of 250 cc. of infusion fluid per kgm. body weight per day was required. The infusion also served to maintain water balance and nutrition as ducks cannot retain food in the normal way under the conditions of the test. With larger volumes of fluid than the above the ducks became oedematous. Details of the method regarding choice of ducks, immobilization of the birds and construction of the pump used should be consulted in the original. Briefly after immobilization a 22-gauge needle is inserted into the leg vein of a duck and secured. It is connected to an individual pump, six of which are fitted to a common shaft which makes 7 revolutions per hour. The pumping action is effected by two rollers mounted opposite one another which compress a rubber tube between them and expel its contents through an outlet while behind them it is refilled from an inlet and a continuous flow of fluid can be maintained. The mechanism proved simple and dependable. The drug was dissolved under sterile conditions in an isotonic solution containing 1.2 per cent. of sodium citrate and 4.2 per cent. of glucose adjusted to pH 7 by hydrochloric acid. One bird in each series received infusion without drug and the concentration of the latter for the other birds was calculated after consideration of all the factors. Each bird was infected intravenously from a donor bird with a dose of  $3 \times 10^9$  parasitized cells per kgm. body weight. Parasite counts and other relevant data were made daily. The minimum effective dose of a drug is defined as that necessary to reduce the number of parasites in a treated bird to half that in a control bird, on the third day when the experiment ended. The following is the author's summary —

- 1 A method incorporating a simple rotary injection pump is described for continuous intravenous administration of drugs to ducks infected with *P. lophurae*.
- 2 On the basis of dosage quinine was more effective at the level of minimum therapeutic response when given intravenously in single daily doses than when given by continuous infusion at a high level of response the converse was true.
- 3 At the level of minimum response cinchonine was equally effective when given in single daily intravenous doses or continuously.
- 4 Tartar emetic, sodium antimony thioglycollate and mapharsen were effective in doses at or near the toxic level.

5 Penicillin streptomycin, and quinine were inactive in the doses employed.

6. Summation of therapeutic response was shown by the following two combinations quinine-cinchonine, and quinaquine-8-chloro-9-(2-diethylamino-ethylamino)-2-methoxyacridine. No summation of response was exhibited by the following combinations quinine-quinaquine quinine-pamaquine and quinaquine-pamaquine. These results suggest that quinine quinaquine and pamaquine each possess a different principal mechanism of drug action against *P. lophurae* in the duck.

J. D. Fulton

TALIAFERRO W. H. Immunity in Malaria. *Amer J Clin. Path.* 1944 Dec., v 14 No 12, 563-7 [23 refs.]

This is an interesting article which might be entitled "An Introduction to the study of Immunity in Malaria." It reviews the knowledge which has been acquired chiefly from the study of the course of infections of *Plasmodium brasilianum* a quartan parasite of New World monkeys in which the author has played a prominent part.

In the first place the infection increases acutely in intensity till as many as 10 per cent. of the red blood corpuscles are infected. This acute rise is terminated by a parasite decline at times so sudden as to justify the application of the term crisis. This is followed by a low-grade infection and finally by latency when no parasites can be found in thick blood films. This latency is interrupted by frequent relapses of varying severity as occurs with all quartan parasites. In man *P. vivax* has a similar course but the relapses are less frequent than with *P. malariae*. In the case of *P. knowlesi* in rhesus monkeys however the infection develops rapidly during the course of a week till as many as 80 per cent. of the red cells are infected, a result which is nearly always fatal. Occasionally there is a terminal reduction in the number of parasites but this is insufficient to ward off the fatal issue. By treatment however the infection can be reduced so that a condition of low-grade infection, or latency is reached. In many respects *P. knowlesi* though of tertian periodicity resembles *P. falciparum* in man.

Natural immunity to *P. brasilianum* is exemplified by the fact that in first infections 6 to 8 of the 9 merozoites produced at each schizogony are destroyed before red cells are invaded and of those that succeed in establishing themselves half fail to become mature schizonts. This rate of destruction, which is largely a phagocytic phenomenon is greatly increased when there is an acquired immunity. The destruction of the parasites is correlated with the phagocytosis of free parasites and infected red corpuscles chiefly in the spleen liver and bone marrow. This is particularly marked in the spleen where filtration of infected cells occurs in the Billroth cords as the result of the action of a specific agglutinin. This is followed by opsonization which stimulates phagocytosis. In *P. falciparum* infections the infected cells are often agglutinated in other organs for instance in the brain or placenta with the result that the phagocytic cells the macrophages become active in these unusual sites. The most reasonable explanation of the increased activity of macrophages in acquired immunity is that they and the parasites are influenced by a specific opsonin. It has been shown by COGGERHALL and KUMAR (this Bulletin 1933 v 35 109) that acquired immunity to *P. knowlesi* can be passively transferred with immune serum. In addition to the development of antibodies during acquired immunity certain non-specific factors operate. There is a tremendous hyperplasia of macrophages and lymphoid cells chiefly in the spleen and bone marrow. These new macrophages arise from division of pre-existing macrophages or from lymphocytes and monocytes.

The results obtained in the study of monkey malaria have their parallel in human malaria. Certain races have a higher natural immunity than others while acquired immunity has been clearly demonstrated in man under experimental conditions. Absolute immunity is difficult to acquire because the immunity is strain-specific. The largest number of strains is found in *P. vivax* and the smallest number in *P. malariae*. In any case when there is an acquired immunity this is largely if not entirely associated with a latent or low grade infection which is liable to relapse at any time. Attempts have been made to induce artificial immunization passively or actively in monkeys and birds with some success but this procedure offers little promise in man. On the other hand, though there is little to suggest that artificial immunity can be employed to protect man there is little doubt that it is an adjuvant in drug treatment. The mechanism of relapse is not known though there is an increasing tendency to ascribe this to the persistence during latency of exoerythrocytic stages. These lead to infection of erythrocytes which are destroyed so long as immunity persists. When this immunity subsides the erythrocytic development progresses unhindered, sometimes with serious results.

Other serological changes occur during malarial infections. Thus antibodies including precipitins agglutinins and complement-fixing substances are produced. From the immunological standpoint it is of interest that complement fixation depends on a genus antigen and is thus very different from acquired immunity which is species and strain specific. Thus effective complement-fixing antigens for human malaria have been prepared from *P. knowlesi* and *P. gallinaceum*. The various points mentioned in this summary in their bearing on the epidemiology treatment and control of malaria are discussed in the paper which is rendered all the more valuable by the author's careful reference to the original papers upon which his statements are based. C M Wenyon

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## BLACKWATER FEVER.

KITCHEN S F & SADLER G G Report of an Attack of Blackwater Fever subsequent to Induced Malaria. *Amer J Trop Med* 1945 Sept. v 25 No 5 379-84 3 figs.

The authors describe in detail the occurrence of blackwater fever in a female patient in whom malaria was induced by the introduction of three plasmodial species in succession viz. *P. vivax*, *P. falciparum* and *P. malariae*. The *P. vivax* infection was characterized by 27 quotidian paroxysms and spontaneous termination. Occasional parasites were seen in the peripheral blood several months later but without clinical signs of malaria. Six months after the termination of the *P. vivax* attacks a natural inoculation of *P. falciparum* was given. The resulting malaria was treated with quinine. Five weeks later *P. malariae* infection was induced by intravenous injections of infected blood. This infection was terminated by plasmoquin six weeks later *P. falciparum* persisted in the peripheral blood in spite of these treatments. There were waves of parasitaemia with only occasional clinical signs of malaria, for nearly five months. At the end of this period the patient was given two seven-grain doses of quinine in a single day, the last dose being given at 6 p.m. She refused her evening meal and vomited in the early morning. At 7 a.m. it was noticed that she was jaundiced, and by noon her temperature had reached 103°F

"Late that afternoon" she passed urine containing haemoglobin. There was no rigor associated with the haemoglobinuria. Thereafter the clinical condition was that of typical blackwater fever and rigors were experienced on the sixth and seventh days. There was no oliguria. The urine during the lytic phase was characteristic in appearance. The reaction is not given. She had only one lytic phase and recovered rapidly. *P. falciparum* was not observed in the blood from the onset until the third day after the subsidence of the fever. Treatment included infusions of 5 per cent. glucose in physiological saline, and 50 per cent. glucose from the first day. Transfusions of 500 cc. of citrated blood were given on the first, second, fourth and seventh days. The red blood cell count was 0.89 million per cubic mm. on the first day and rose to 1.2 million per cubic mm. on the seventh day. The intake of fluid was carefully balanced throughout against the output in the urine. Sodium bicarbonate was given by mouth in doses of 1 gm. every four hours on the first day.

The chief interest of this case lies in the malarial history. All these strains were well known and had frequently been used for therapeutic purposes. None had any previous record of having been associated with haemoglobinuria.

The authors suggest that the prolonged parasitaemia resulting from the *P. falciparum* malaria may have been an aetiological factor in the production of the haemoglobinuria. They also point out the relationship of quinine administration to the haemoglobinuria attack, as the clinical history of the patient indicates that haemolysis commenced within 12 hours of the administration of the first dose of quinine.

They discuss the treatment from the point of view of replacement of blood by transfusion (they estimate that about three-quarters of the patient's cells were lysed in less than 24 hours) and the administration of alkali. They consider that "the hypothesis that oliguria and anuria are the result of blockage of the renal tubules by haemoglobin degradation products... is open to doubt," and conclude that "the indiscriminate use of intensive alkaline therapy is contra-indicated in blackwater fever."

[The legends for Figures 2 and 3 have been accidentally transposed in the printing of this paper.]

B G Macgrath

LANCET 1945 Dec 1 701-4 1 chart. [23 refs.] Effect of Large Doses of Alkali on Kidney Function. [Army Malaria Research Unit, Oxford (Macgrath B G et al.)]

Intensive alkali treatment is still being recommended for the treatment of blackwater fever incompatible blood transfusion and the crush syndrome. The Medical Research Council recommended that in the treatment of wound shock all cases should be given sodium bicarbonate 7 gm (about 2 drachms) hourly by mouth until the urine turns red litmus blue but not for longer than 24 hours. Intensive alkali therapy of this kind is accompanied by dangers. Experiments described in this paper show that alkali administered for 24 hours to normal subjects at less than half the rate recommended above produces sodium and water retention and disturbance of renal function, which becomes well-marked if the alkali is continued for 72 hours.

Three subjects were given sodium bicarbonate, grams 60 and sodium citrate grains 60 3-hourly, one subject for one day, two for three days. All had disturbance of renal function—in one on the 3-day course this was well marked and led to a three-fold increase of blood urea. All developed sodium and water retention. There was dilution of the blood by about 10 per cent.

The authors consider that large doses of alkali should not be administered in conditions where renal failure may supervene.

Norman White

- i. OSMAN A. A. Effect of Large Doses of Alkali on Kidney Function. [Correspondence.] *Lancet* 1946 Jan 26 143-4
- ii. LOCKET S. Effect of Large Doses of Alkali on Kidney Function. [Correspondence.] *Ibid* Feb 2 180-81

i. OSMAN considers the conclusion of the Malaria Research Unit Oxford that large doses of alkali should not be administered in conditions where renal failure may supervene to be an overstatement. A closely reasoned argument ends thus. Alkali therapy in renal disease certainly has limitations. It is contra-indicated in the earlier stages of acute nephritis for example, but I have generally found that when failure with this method is attributed to its unsuitability it is as often due to faulty technique. I submit that large doses of alkali, when properly used are not necessarily contra indicated in conditions where renal failure may supervene as a natural development of the disease but that given with caution they will sometimes be the only means of saving or prolonging life.

ii. LOCKET considers the findings of the Malaria Research Unit Oxford to be insufficient to justify the conclusions based thereon. The title of their paper is somewhat misleading as only sodium salts were investigated potassium and other alkaline salts were not considered. He does not consider the evidence adduced sufficient to justify the deduction that renal function was impaired in the three experimental subjects

Norman White

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## TRYPANOSOMIASIS

STEFANOPOULO G CAUBET P & DUVOLOK S Mlle Méningoencéphalite à *Trypanosoma gambiense* (souche neurotrope) observée chez le lapin. [Meningo-Encephalitis due to *T. gambiense* in the Rabbit.] *Bull Soc Path Exot* 1945 v 38 Nos. 9/10 271-4 4 figs. on 2 pls

The Yaunde strain [this *Bulletin* 1946 v 43 312] of *Trypanosoma gambiense* in the blood of a rat was injected subcutaneously into the same rabbit on June 1 1943 October 19 1943 November 3 1943 and November 20 1943 during observation for a year the rabbit showed no signs of illness and its weight remained about the same. On June 30 1944 paralysis of the hind quarters developed and soon extended to the forelimbs the rabbit was killed on July 5 1944

At autopsy the spleen was found to be rather small the urinary bladder was distended with 160 cc. of urine and the membranes of the brain were much congested. No trypanosomes were seen in fresh blood preparations but they were present in lymphatic gland juice and especially in scrapings of brain tissue in saline. The cerebral membranes showed pachymeningitis with infiltration of lymphocytes and plasmocytes perivascular cellular infiltration was seen in the brain. In sections trypanosomes were fairly numerous in the infiltrated areas of the membranes and some isolated trypanosomes were present in the brain tissue. The general appearance was similar to what is found in sleeping sickness in man. No morular cells of Mott were seen in the brain but a few were present in the spleen. These findings are shown in photomicrographs.

The authors comment that the neurotropic character of this strain shown in the mouse and rat is also apparent in the rabbit

J F Corson

## Tropical Diseases Bulletin

ROUBAUD E. & CAUBET P. Essais d'immunisation chimio-biologique par le sulphasénol dans les infections à *Trypanosoma gambiense* chez le rat. [Attempts at Chemo-biological Immunisation in Infections with *Trypanosoma gambiense* in the Rat.] Bull. Soc. Path. Exot. 1944 v 37 No. 9/10 290-84

Two laboratory strains called Antwerp and Yaounde respectively [see CAUBET this Bulletin 1948 v 43 312] were used and five experiments were made. The object was to see whether rats developed immunity after treatment of *T. gambiense* infections with sulphasénol and, if so to estimate the degree and specificity of the immunity. The rats were infected by intra peritoneal or subcutaneous inoculation, and sulphasénol was injected as soon as trypanosomes were found in the peripheral blood. After varying intervals the immunity was tested by inoculation of one or other of the two strains of *T. gambiense* and also in one experiment by injection of *T. cruzi*. The doses of sulphasénol are expressed as per 100 gm body weight.

**Experiment 1**—Five white rats were inoculated with the Antwerp strain injected and sterilized the peripheral blood 48 hours and 0.03 gm. of sulphasénol was injected and sterilized the peripheral blood. After 70 days interval, 15 000 trypanosomes of the Antwerp strain were inoculated intraperitoneally two untreated rats and two others which had been injected with the same dose of trypanosomes. The untreated controls showed trypanosomes on the 4th day and these were numerous on the 10th day. The control which received sulphasénol 70 days before behaved similarly while the control which had received the drug 20 days before was not infected. Of the 5 experimental rats, two behaved like the untreated controls while the other 3 developed a slow irregular infection which did not become acute until 13 to 20 days later than in the controls.

**Experiment 2**—Three experimental rats and 2 untreated control rats were used. The same procedure as in the first experiment was carried out but the interval was 80 days and the test dose was 500 trypanosomes. The 3 rats became infected but much more slowly than the controls.

**Experiment 3**—A rat of experiment 1 (2) infected with the Antwerp strain in spite of treatment with 0.01 gm. of sulphasénol 90 days before, was given a second injection of 0.01 gm. of sulphasénol to reinforce its immunity after 40 days. 200 trypanosomes of the Antwerp strain were injected. Trypanosomes appeared in the blood on the 5th day but the infection was chronic, with few trypanosomes in the blood and the rat died on the 80th day whereas the control rat died of an acute infection on the 60th day.

**Experiment 4**—Two rats infected with the Antwerp strain and sterilized by an injection of 0.015 gm. of sulphasénol were tested after 80 days with a dose of 400 trypanosomes of the Yaounde strain injected subcutaneously. 2 untreated rats serving as controls. The controls showed trypanosomes on the 12th and 25th days respectively and the former died with an acute infection after a month. The experimental rats showed trypanosomes on the 23rd and 41st days respectively and the latter died on the 60th day (the times of death of the other control rat and the other experimental rat are not stated).

**Experiment 5**—Two rats were injected with 0.03 gm. of sulphasénol and 75 and 90 days later (75 & 90 days) were infected with the Antwerp strain. They then received a second injection of 0.014 gm. of sulphasénol, one 10 days and the other 30 days after the appearance of *T. cruzi* one after 30 days and were inoculated with 1,000 trypanosomes of the trypanosomes. Finally they the other after 60 days, two untreated control rats being also injected. All four

animals responded similarly they showed trypanosomes at 5 to 8 days and died at 11 to 12 days

The authors remark that the protection was relative only and was apparently specific for *T. gambiense* even though the two strains showed pathogenic differences. There were indications that the destruction of trypanosomes in the tests with injection of 15 000 produced some toxæmia. [It seems to the abstracter that more rats might have been used with advantage.]

J F Corson

ROUBAUD E. A propos des caractéristiques raciales des souches de *Trypanosoma gambiense* [Racial Characters of Strains of *Trypanosoma gambiense*] *Bull Soc Path Exot* 1944 v 37 Nos 9/10 290-91

The author refers to CAUBET's measurements of two strains of *T. gambiense* [see this *Bulletin* 1946 v 43 312] and asks whether such different strains exist in nature or are artificially produced by long maintenance in laboratory animals. The characters of the Yaunde strain have never varied since its isolation and it has never become completely adapted to the blood of small rodents: this suggests that it is a special racial type with marked neurotropic characters [see below]

Perhaps a selection occurs in man when the infection passes from the early stage in the blood and lymphatic glands to the later stage with involvement of the central nervous system: these selected races might be spread by tsetse flies in nature. This could explain the variations between the clinical picture and the number of cases [*gravité relative de l'endémie*] often observed in sleeping sickness areas. KUNERT [this *Bulletin* 1940 v 37 17] noted earlier infection than formerly of the nervous system in *T. rhodesiense* infections in man and Roubaud suggests that this might be explained by the predominance of neurotropic strains: since in such infections trypanosomes are rare in the peripheral blood the infection would be less transmitted by tsetse with the result that the amount of sleeping sickness in the area would diminish while the virulence for the nervous system would increase. The question deserves attentive study.

J F Corson

ROUBAUD E. STEFANOPOULO G J & DUVOLOU S Mlle. Étude chez le rat blanc d'une souche neurotrophe de *Trypanosoma gambiense* [A Study of a Neurotropic Strain of *T. gambiense* in the White Rat.] *Bull Soc Path Exot* 1944 v 37 Nos 9/10 292-6 3 figs (2 on 1 pl.) [10 refs.]

During 1943 twelve white rats were infected from guinea-pigs, mice or other rats with the Yaunde strain of *T. gambiense*. Three died of the disease after 31, 37 and 54 days and six were killed after 55, 66, 68, 77, 77 and 82 days. The incubation period varied from 4 to 45 days. In the blood the trypanosomes were few and were often absent and in only three rats were trypanosomes very numerous at the time of death. In several rats trypanosomes were found at autopsy only in the central nervous system and in some in the lymphatic glands also. Two rats were inoculated intracerebrally and both became paralysed and were killed after 79 days: one only had shown trypanosomes (very few) in the blood on the 17th and 74th days but they were very numerous in the brain in both rats. In most cases there was little fever. The body weight remained stationary except in young rats where slight increase occurred and in infections of long duration where marked wasting took place. Four out of 5 rats in which the infection had lasted for more than two months showed severe nervous symptoms—tremors, staggering, spasms or contractures, paresis or paralysis of the limbs or sphincters.



At autopsy the spleen usually showed little enlargement but the lymphatic glands were very often hypertrophied and sometimes congested. The histological appearances of most interest were in the central nervous system. 7 out of 11 rats showed meningoencephalitis similar to that described in the mouse by STEFANOPOULO and ÉRÉVÉ [this *Bulletin* 1945 v 42, 258]. This was seen especially in rats killed after the 60th day. There was intense perivascular infiltration chiefly of plasmocytes, the neurones frequently showed damage and neuronophagia was observed, especially in the two rats which were inoculated intracerebrally. Trypanosomes were seen in the brain substance in three cases. In one of those inoculated intraperitoneally which was killed on the 68th day the blood showed a few trypanosomes but on the 33rd day only. The other organs showed the usual lesions such as infiltration of the portal canals of the liver, necrosis and degeneration of some hepatic cells, interstitial infiltration of the kidney, many plasmocytes in the spleen &c. [the heart is not mentioned]. The mulberry cells of Mott were seen in the brain and spleen of some of the rats [see below].

For comparison 12 rats were similarly inoculated with the Antwerp strain [see CAUBET this *Bulletin* 1946 v 43, 312] which produced acute infections. In only one of 7 rats examined were there lesions of meningo-encephalitis.

The authors refer to the work of others [see this *Bulletin* 1945 v 42, 258] they regard the Yaounde strain as a race of *T. gambiense* with certain fixed characteristics. J. F. Corson

JACKSON C. H. N. Pairing of *Glossina morsitans* Westwood with *G. swynnertoni* Austen (Diptera). *Proc. Roy. Entom. Soc. London*. Ser. A. Gen. Entom. 1945 Dec 31 v 20 Pts 10-12, 168.

It is already known that in cages males of *Glossina morsitans* or *swynnertoni* mate at random with females of either species and do not select those which are co-specific.

The author has carried out a field experiment to examine the same point. He worked in a spot in which *G. swynnertoni* was abundant and exposed large numbers of pupae of both species in such a way that the adults on emergence were completely free. He caught several hundred pairs and studied the proportion in which the two individuals were of the same or different species. He concludes that even in nature male *G. swynnertoni* mates at random with females of its own species or *morsitans*. The same is probably true of male *G. morsitans* but the numbers were lower and the result not conclusive.

This is remarkable for it has been shown by VANDERPLANK [this *Bulletin* 1945 v 42, 89] that heterogamous matings are barren or nearly so, yet neither species has any mechanism to prevent this occurrence. P. A. Buxton.

STEFANOPOULO G. CAUBET P. & DUVOLOX S. Mlle. Présence de cellules muliformes de Mott chez les rats infectés de *Trypanosoma gambiense*. [The Mulberry Cells of Mott in Rats Infected with *Trypanosoma gambiense*] *Bull. Soc. Path. Exot.* 1944 v 37 Nos 9/10 296-300 4 figs on 1 pl. [17 refs.]

The "mulberry cells" of Mott were found in the tissues of 2 out of 11 white rats infected with the Yaounde strain of *T. gambiense*. In one rat they were present in the splenic pulp amid numerous plasmocytes. In some mulberry cells the nucleus had disappeared but in others the plasmocyte character of the cell was recognizable, i.e. eccentric nucleus radiating spoke-like chromatin and basophilic cytoplasm with vacuoles or globules polygonal from mutual pressure which stained rose-violet with Giemsa's stain. Many intermediate

forms between the plasmocvte and the typical mulberry cell were seen. In sections of the brain of the second rat there were lesions of meningo-encephalitis intense perivascular infiltration and trypanosomes in the brain tissue. Mott's cells were seen both in the infiltrations and in the brain tissue some were stained a rose colour by Giemsa's stain and others were unstained fuchsin stained them a bright red colour. These cells were also present in the spleen of this rat.

Impression films were made of the organs of 6 other rats similarly infected and mulberry cells were found in two of them in the liver and spleen these cells stained a pale blue a difference from those in sections which was noted by REICHENOW (*Ztschr f Hyg u Infektionskr* 1921 v 94 266). They were also found in impression films of the organs of guinea-pigs and mice infected with this strain of *T. gambiense*.

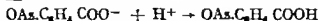
In discussion LAYTER emphasized the value of staining with fuchsin to distinguish Mott's cells from other very similar cells such as macrophages packed with refractive inclusions. He and others who took part in the discussion considered that Mott's cells are not pathognomonic of trypanosomiasis. CAPPONI referred to their presence in *T. lewisi* infections of the brown rat in Marseilles observed by ARGUE and himself in 1943.

J. F. Corson

EAGLE H. The Spirochaetidal and Trypanocidal Action of Acid-substituted Phenyl Arsenoxides as a Function of pH and Dissociation Constants. *J. Pharm & Exper Therap* 1945 Nov v 85 No 3 265-82 8 figs [24 refs.]

In earlier papers Eagle and his associates described the action of a number of substituted phenyl arsenoxides on spirochaetes (*J. Pharm & Exper Therap* 1940 v 70 221) and trypanosomes [this *Bulletin* 1945 v 42, 15]. With only a few exceptions acid substitution caused a marked decrease in activity of the parent arsenoxide and in the present very interesting contribution Eagle produces considerable evidence for the view that this diminished activity is to be explained on the basis that the ionized salts of these substituted compounds are relatively inactive as compared with the undissociated free acids. This is in line with the facts (a) that the dissociation constants of most of these compounds are such that they would be more than 99 per cent ionized at pH 7.4 and (b) that increase in the hydrogen ion concentration of the medium in which the tests are conducted results in increased spirochaetocidal or trypanocidal activity.

With regard to (b) above, the most obvious effect of increasing the hydrogen ion concentration consists in the formation of undissociated free acid from the ionized salt e.g. —



If the inference is correct that the undissociated acid is many times more active than the charged ion there should be a close correlation between the trypanocidal activity of an acid-substituted compound at a given pH and the pH of that compound. The higher the pK (i.e. the weaker the acidic group) and thus the higher the proportion of the undissociated acid at a given pH the greater should be the activity of the compound. This was in fact found by experiment to be the case.

That the striking influence of pH on the trypanocidal and spirochaetocidal activity of acid-substituted phenyl arsenoxides is related to the ionization of the acidic group is borne out by a number of other findings. Thus the activity of the unsubstituted phenyl arsenoxide was largely independent of pH. This is also true of the 3-NH<sub>2</sub>-4OH phenyl arsenoxide in which neither of the substituents is strongly acidic. Still more significant is the fact that when an acidic group is

blocked as by amide formation (e.g. the  $\beta$ -CONH<sub>2</sub> compound) the trypanocidal activity is no longer dependent on pH.

Although the ionized salts of acid-substituted phenyl arsenoxides in general are considered to exercise a relatively low (but variable) degree of activity it is inferred that in a few exceptional instances (as in the  $\beta$ -(CH<sub>3</sub>)<sub>2</sub>COOH compound see this *Bulletin* 1945 v 42, 354) the ion is unusually active. This adding to the activity due to the undissociated molecule accounts for the unexpectedly high activity of these particular compounds.

Eagle finds sufficient correspondence between theoretical calculation and observed fact to warrant the conclusion that the relative trypanocidal activity of an acid-substituted phenyl arsenoxide is determined by and is roughly predictable from—(a) the pH of the solution (b) the  $\beta$ K of the compound (c) the trypanocidal activity of the ion. The higher the  $\beta$ K, and the lower the pH the greater will be the observed activity of the compound.

Arsenic estimations established that the relative inactivity of the salts of these compounds reflected the fact that they were bound to the trypanosomes to only a minor degree while the undissociated free acids like all highly active compounds were concentrated as much as three-hundred-fold. Variations in pH affecting the relative proportions of ions and undissociated acid, similarly affected the degree to which a given arsenical was bound by the trypanosomes. In a series of acid-substituted phenyl arsenoxides those with the highest  $\beta$ K values (most readily transformed to the undissociated acid on acidification) are the first to show increased activity and increased affinity for the trypanosomes as the reacting mixture is acidified while those with strongly acidic groups which remain as ions at the lowest pH tested are correspondingly unaffected with respect to both activity and combining affinity.

The author discusses the question whether the undissociated acid-substituted phenyl arsenoxides are so strongly bound to trypanosomes because they have an especial reactivity with cellular constituents such as those containing SH groups. He concludes however that the explanation most probably lies in the fact that the undissociated acids penetrate readily into the interior of the trypanosome cell, whilst the ionized salts are unable to gain admission. He quotes a number of instances from the literature of widely-separated fields of experimental biology in support of the general contention that the ions of weak acids (or bases) pass through cell membranes less readily than the corresponding undissociated molecules. A distinguishing feature of the trypanosome-arsenical system here studied lies in the speed at which and particularly in the degree to which, active non-ionized arsenicals may be concentrated by the trypanosomes. Within ten minutes the arsenic concentration in the organisms may attain a level several hundred times greater than that of the surrounding fluid. This reflects a rapid diffusion of the arsenical into the organisms, followed by its firm combination with cellular constituents. The arsenical is thereby effectively removed from the diffusion equilibrium, permitting its continued diffusion into the cell. In a sense the organisms promote their own death by binding the active (undissociated acid) form of the compound and thus shifting the equilibrium so as to result in the production of yet more of that active form.

E M Lounie

CHORLEY J. H. Tsetse Fly Operations. Short Survey of the Operations by Districts for the Year ending December 1943. *Rhodesia Agric J* 1944 v 41 No 6 412-19 [Summary taken from *Rev Applied Entom.* Ser B 1946 Jan. v 34 Pt. 1 15]

There was little improvement in the position as regards trypanosomiasis of cattle in the Chipinga area of the Mafsetter District on the eastern border of

Southern Rhodesia, in 1943. The total number of tsetse-flies caught on the Rhodesian side of the border was 20 comprising 11 males and five females of *Glossina pallidipes* Aust. and three males and one female of *G. brevipalpis* Newst while 15 males and 13 females of the former and one male and two females of the latter were taken in the clearing on the Portuguese side. Extensive additions were made to the main border clearing. Patrols carried out in Portuguese East Africa and on the border farms indicated that *G. morsitans* has not spread much further up the Busi Valley though individuals were caught about one mile from the border. A light infestation of this species was found in the lower Sabi Valley inside Southern Rhodesia during the year hood. It is not anticipated that the Sabi and Lundi Rivers will act as effective barriers to the westward spread of the fly as they carry little water in the dry season. The Portuguese Government has declared a large area in Portuguese East Africa along the border east of the Melsetter district an open area for the destruction of all classes of game. This may have highly beneficial results in the control of *G. morsitans* if intensive shooting operations can be organised. The presence of tsetse on the border in the Vila Gouveia area of Portuguese East Africa opposite Inyanga has been notified. Satisfactory progress was made in the northern areas infested by *G. morsitans* fly densities over the whole area covered by the operations showing a progressive reduction. No cases of animal trypanosomiasis were recorded from these areas. *G. pallidipes* was found to occur some distance south of its previously known limits in the Sebungwe district. The north-eastern boundary of the area remains heavily infested. Eight more cases of sleeping sickness were recorded from the Urungwe district three foci of the disease being now recognised. The situation in individual districts is briefly reviewed and incidental aspects of tsetse control are discussed.

LAUNOY L. Albuminurie de la trypanosomose expérimentale à *T. annamensis* du lapin action des agents trypanocides. I. Action du moranyl employé seul. [The Action of Trypanocidal Agents on the Albuminuria of Experimental Infection with *Trypanosoma annamense* in the Rabbit. L. The Action of Moranyl alone.] Bull Soc Path Exot 1944, 37 Nos. 11/12 347-58 4 graphs

Different opinions have been expressed on the importance of the albuminuria which often occurs during the treatment of human trypanosomiasis with Bayer 205 as the author could always cause albuminuria in rabbits by infecting them with his strain of *T. annamense* he decided to make experiments to get an answer to two questions (1) Can moranyl [Bayer 205] cause albuminuria in a rabbit with healthy kidneys? (2) what effect has treatment with moranyl on the albuminuria of trypanosomiasis?

He first injected various amounts of moranyl at various intervals into rabbits (4) and estimated the albumin urea and chlorides in the urine. slight albuminuria was produced but it soon disappeared. He then infected rabbits (3) with *T. annamense* and treated them with moranyl this cured the infection and the albuminuria also disappeared. The figures of the excretion of urea and chlorides gave no indication of serious damage to the kidney having been produced. Details of the experiments are given.

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E. M. LOURIE

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per kgm. have little toxic action on the kidneys. Trypanosomiasis causes albuminuria 2 to 3 weeks after infection. It is cured by moranyl before the drug produces its slight irritant effect on the kidneys. These experiments offer no evidence that albuminuria due to trypanosomiasis is a contraindication to treatment with moranyl alone.

J. F. Corson

LAUNOY L. L'albuminurie de la trypanosomose expérimentale à *T. annae* chez le lapin: action des agents trypanocides. II. Action de la synergie moranyl-anthiomaline. [The Action of Trypanocidal Agents on the Albuminuria of Experimental Infection with *T. annae* in the Rabbit. II. The Action of Moranyl and Anthiomaline.] *Bull. Soc. Path. Exot.* 1945 v 38 Nos. 9/10 275-8.

The course of an infection of *Trypanosoma annae* in a rabbit and the effects of treatment with moranyl and anthiomaline, administered simultaneously, are recorded in full detail. Treatment was delayed until the 47th day after inoculation, the animal being then very ill. The effects were similar to those produced in previous experiments with treatment by moranyl alone [above]. The two drugs were injected together, anthiomaline intramuscularly and moranyl subcutaneously, on the 47th, 51st and 57th days of infection; on the 60th day an injection of trypanamide was given. Albuminuria soon disappeared and the rabbit quickly recovered. The author concludes that synergic treatment with anthiomaline and moranyl in suitable dosage is not contraindicated by the presence of albuminuria.

J. F. Corson

RODHAIN J. & RESSLER, R. Essai de différenciation sérologique entre trypanosomes et schizotrypanosomes. [An Attempt to differentiate serologically between Trypanosomes and Schizotrypanosomes.] *Ann. Soc. Belge de Méd. Trop.* 1945 June 30 v 25 Nos. 1/2 23-37.

The only species of trypanosomes which multiply within the cells of the vertebrate host are *T. cruzi* and *T. pipistrelli* (of the bat); they multiply by binary fission, not by schizogony. The authors made serological tests to see whether these species could be distinguished in this way from other species of trypanosomes: they used *T. brucei* maintained for several years in mice and rats, *T. cruzi* maintained in a species of bug (*Reduvius prolixus* (fumatus)), and in guinea-pigs, *T. pipistrelli* in culture and *T. vesperilionis* also in culture, and they had also a rabbit infected with *T. equiperdum*. To obtain specific antisera rabbits were infected with *T. brucei* and with *T. cruzi* and injections of large total amounts (nearly 100 cc.) of cultures of *T. vesperilionis* and of *T. pipistrelli* into rabbits were made during several weeks. The tests used were complement fixation, precipitin reaction and agglutination: the details are shown in tabular form.

All the precipitin tests were negative: the complement fixation tests indicated that there was an antigenic relationship between *T. cruzi* and *T. vesperilionis*, less between *T. cruzi* and *T. equiperdum* and still less between *T. cruzi* and *T. pipistrelli*. The agglutination tests indicated that *T. cruzi* and *T. pipistrelli* had a common agglutino-gen which was not present in *T. vesperilionis*.

The only final conclusion was that the two species of trypanosome (*Schizotrypanum*) which multiply within the cells of the vertebrate host cannot be distinguished from other trypanosomes by serological tests.

J. F. Corson

BARRETO A. L. de B. & PONDÉ A. Doença de Chagas na Bahia. Dois casos parasitologicamente confirmados. [Chagas's Disease in Bahia: Two Cases.] *Brasil-Médico.* 1945 Nov. 17 & 24 v 60 Nos. 46/47 394-7 6 figs.

## LEISHMANIASIS

ARMSTRONG T G Asymptomatic Kala-Azar in Soldiers from Over-Seas  
*Brit Med J* 1945 Dec. 29 918

Two cases are described in which fever was slight and toxæmia absent with the result that kala azar remained for some time unsuspected. The first was in a soldier 20 years of age who served for a year in N Africa before transfer to Salerno and Naples. Eighteen months after leaving N Africa he was ordered by his sergeant to report sick. On being questioned he admitted a slow onset during five months of malaise, loss of weight and lassitude and he was easily fatigued. He was thin and anaemic with a low-grade pyrexia up to 99°F. The spleen was so soft that several weeks elapsed before the author finally decided that it was actually enlarged. In view of a leucopenia and granulopenia, a marrow puncture was performed, with the result that leishmania were discovered. Under stilbamidine treatment the patient made a slow and uneventful recovery.

The second patient returned to England in January 1944 after a year's service in N Africa, being invalided for diphtheritic polyneuritis. He recovered completely from this and finally came up for demobilization in September 1945 when he was found to have a greatly enlarged spleen. He made no spontaneous complaint, but on being questioned admitted some dyspnoea on exertion. Examination showed few if any signs apart from those attributable to the large spleen which extended well below the umbilicus. There was a low red cell count and a leucopenia. Marrow puncture showed leishmania which were also found by inguinal gland puncture.

The author points out that cases of kala azar are likely to be encountered occasionally in England and that unless the disease is borne in mind it may easily be overlooked. In both the cases described the patients when pressed admitted minor symptoms of several months duration, but these they had regarded as so slight as not to warrant attendance at sick parade.

C M Wenyon

SEN GUPTA, P C. Complement-Fixation Test with Witebsky, Klingenstein, Kuhn (WKK) or similar Antigens: a Modified Technique. *Indian Med Gaz* 1945 Aug v 80 No 8 396-8

In previous papers [this *Bulletin* 1944 v 41 17 1945 v 42 358] the author has given an account of his experiences with the complement fixation test for kala azar when the WKK antigen prepared from the acid fast bacilli of KEDROWSKY and of LLERAS was employed. His further experience has shown that a certain modification of the technique ensures more reliable results. This involves the titration of antigen and complement in a 1:25 dilution of serum instead of in saline and ensures that the titration is made under the conditions that exist in the test proper. It is confirmed that in the absence of severe leprosy and post kala azar dermal leishmaniasis a positive result is indicative of kala azar. A negative reaction is given by only 1 per cent. of all untreated cases in Calcutta and these appear to be very early cases. The fact that a small number of obvious cases of chronic pulmonary tuberculosis give a positive reaction cannot obscure the diagnosis.

Those who wish to carry out the test must consult the original article for full details of the technique.

C M Wenyon



per kgm. have little toxic action on the kidneys. Trypanosomiasis causes albuminuria 2 to 3 weeks after infection. It is cured by moranyl before the drug produces its slight irritant effect on the kidneys. These experiments offer no evidence that albuminuria due to trypanosomiasis is a contraindication to treatment with moranyl alone.

J F Corson.

LAUNOY L. L'albuminurie de la trypanosomose expérimentale à *T. cruzi* du lapin: action des agents trypanocides. II. Action de la synergie moranyl-anthiomaline. [The Action of Trypanocidal Agents on the Albuminuria of Experimental Infection with *T. cruzi* in the Rabbit. II. The Action of Moranyl and Anthiomaline.] *Bull. Soc. Path. Exot.* 1945 v 38 No. 9/10 275-8.

The course of an infection of *Trypanosoma cruzi* in a rabbit and the effects of treatment with moranyl and anthiomaline, administered simultaneously, are recorded in full detail. Treatment was delayed until the 47th day after inoculation, the animal being then very ill. The effects were similar to those produced in previous experiments with treatment by moranyl alone [above]. The two drugs were injected together: anthiomaline intramuscularly and moranyl subcutaneously on the 47th, 51st and 57th days of infection. On the 60th day an injection of trypanamide was given. Albuminuria soon disappeared and the rabbit quickly recovered. The author concludes that synergic treatment with anthiomaline and moranyl in suitable dosage is not contraindicated by the presence of albuminuria.

J F Corson.

RODMAN J & RESSLER, R. Essai de différenciation sérologique entre trypanosomes et schizotrypanosomes. [An Attempt to differentiate serologically between Trypanosomes and Schizotrypanosomes.] *Ann. Soc. Belge de Méd. Trop.* 1945 June 30 v 25 No. 1/2, 23-37.

The only species of trypanosomes which multiply within the cells of the vertebrate host are *T. cruzi* and *T. pipistrelli* (of the bat): they multiply by binary fission, not by schizogony. The authors made serological tests to see whether these species could be distinguished in this way from other species of trypanosomes: they used *T. brucei* maintained for several years in mice and rats; *T. cruzi* maintained in a species of bug (*Reduvius prolixus* (*formatus*)) and in guinea-pigs; *T. pipistrelli* in culture and *T. vespertilionis* also in culture, and they had also a rabbit infected with *T. equiperdum*. To obtain specific antisera rabbits were infected with *T. brucei* and with *T. cruzi* and injections of large total amounts (nearly 100 cc.) of cultures of *T. vespertilionis* and of *T. pipistrelli* into rabbits were made during several weeks. The tests used were complement fixation, precipitin reaction and agglutination: the details are shown in tabular form.

All the precipitin tests were negative: the complement fixation tests indicated that there was an antigenic relationship between *T. cruzi* and *T. vespertilionis*, less between *T. cruzi* and *T. equiperdum* and still less between *T. cruzi* and *T. pipistrelli*. The agglutination tests indicated that *T. cruzi* and *T. pipistrelli* had a common agglutinogen which was not present in *T. vespertilionis*.

The only final conclusion was that the two species of trypanosome (*Schizotrypanum*) which multiply within the cells of the vertebrate host cannot be distinguished from other trypanosomes by serological tests.

J F Corson.

BARRETO, A. L. de B. & POYET, A. Doença de Chagas na Bahia: Dois casos parasitologicamente confirmados. [Chagas's Disease in Bahia: Two Cases.] *Brasil-Médico.* 1945 Nov. 17 & 24 v 69 No. 46/47 394-7 6 figs.

## LEISHMANIASIS

ARMSTRONG T G Asymptomatic Kala-Azar in Soldiers from Over-Sea  
*Brit Med J* 1945 Dec 29 918

Two cases are described in which fever was slight and toxæmia absent with the result that kala azar remained for some time unsuspected. The first was in a soldier 20 years of age who served for a year in N Africa before transfer to Salerno and Naples. Eighteen months after leaving N Africa he was ordered by his sergeant to report sick. On being questioned he admitted a slow onset during five months of malaise, loss of weight and lassitude and he was easily fatigued. He was thin and anaemic with a low-grade pyrexia up to 99°F. The spleen was so soft that several weeks elapsed before the author finally decided that it was actually enlarged. In view of a leucopenia and granulopenia a marrow puncture was performed with the result that leishmania were discovered. Under stilbamidine treatment the patient made a slow and uneventful recovery.

The second patient returned to England in January 1944 after a year's service in N Africa being invalided for diphtheritic polyneuritis. He recovered completely from this and finally came up for demobilization in September 1945 when he was found to have a greatly enlarged spleen. He made no spontaneous complaint but on being questioned admitted some dyspnoea on exertion. Examination showed few if any signs apart from those attributable to the large spleen which extended well below the umbilicus. There was a low red cell count and a leucopenia. Marrow puncture showed leishmania which were also found by inguinal gland puncture. The author points out that cases of kala azar are likely to be encountered occasionally in England and that unless the disease is borne in mind it may easily be overlooked. In both the cases described the patients when pressed admitted minor symptoms of several months duration but these they had regarded as so slight as not to warrant attendance at sick parade.

C M Wenyon

SEN GUPTA P C Complement-Fixation Test with Witebaky, Klingenstein,  
 Kuhn (WKK) or similar Antigens a Modified Technique. *Indian Med*  
*Gaz* 1945 Aug v 80 No 8 396-8

In previous papers [this *Bulletin* 1944 v 41 17 1945 v 42 358] the author has given an account of his experiences with the complement fixation test for kala azar when the WKK antigen prepared from the acid fast bacilli of KEDROWSKY and of LLERAS was employed. His further experience has shown that a certain modification of the technique ensures more reliable results. This involves the titration of antigen and complement in a 1:25 dilution of serum instead of in saline, and ensures that the titration is made under the conditions that exist in the test proper. It is confirmed that in the absence of severe leprosy and post kala azar dermal leishmaniasis a positive result is indicative of kala azar. A negative reaction is given by only 1 per cent of all untreated cases in Calcutta and these appear to be very early cases. The fact that a small number of obvious cases of chronic pulmonary tuberculosis give a positive reaction cannot obscure the diagnosis. Those who wish to carry out the test must consult the original article for full details of the technique.

C M Wenyon

## FEVERS OF THE TYPHUS GROUP

Lusk, J W. One Hundred and Fourteen Cases of Typhus Fever seen in an Indian Military Hospital in Calcutta. *Indian Med Gaz.* 1945 Sept. v 80 No 9 437-45 4 charts. [21 refs.]

This paper illustrates the difficulty so often experienced in India of determining to which vector-subgroup cases of typhus-group fevers belong. The author saw 114 cases during the months June to December 1943 of these 60 came from a village 80 miles from Calcutta and 54 from Calcutta and its environs.

The salient features have been extracted from the text and tables and are shown in tabular form [minor inconsistencies occur in the original tables] —

Serological type	Village cases	Calcutta cases	Total fatal
OXA	65 (4 fatal)	41 (7 fatal)	11
O119	3	9	0
O12	0	1 (fatal)	1
Clinical and P.M. evidence	2 (2 fatal)	3 (3 fatal)	5

Louse transmission seems to have been excluded, so that although the great majority of the cases can be assumed to have been mite-borne there may have been 12 flea-borne and possibly one or more tick borne cases.

No local lesion was seen in any case and only two patients showed appreciable lymphadenitis. A pronounced rash occurred in the O12 case in which also there was troublesome bleeding from the gums. In 14 other patients all of the OXA type a faint macular rash was detected.

[It would not be helpful to summarize the clinical and other features in detail because these would not be comparable with those seen in purely mite-borne outbreaks.]

John W D Megaw

SNYDER J C ZARAFONTIS C J D & LIU W T. The Susceptibility of the Rodents, *Gerbillus gerbillus* and *Gerbillus pyramidum* to Experimental Typhus Infection. *Proc. Soc. Exper Biol & Med* 1945 June v 50 No 2, 110-12.

Two rodents, *Gerbillus gerbillus* and *Gerbillus pyramidum* especially the were found highly susceptible to inoculation with the rickettsiae of louse-borne and murine typhus. Inoculation with large doses of either strain by nasal intraperitoneal or intravenous routes caused death in most of the animals within 3-8 days. The intravenous route was found most satisfactory.

Animals which had recovered from sub-lethal doses of either strain of rickettsiae were immune to heavy doses of infection by both strains.

*G. gerbillus* after subcutaneous inoculation with two relatively small doses of louse-borne typhus vaccine became immune to a lethal dose of the same strain of rickettsiae.

After sub-lethal doses of either strain of infection, complement-fixation antibodies were found for the homologous strain there was a slight degree of cross fixation.

The Well-Felix reaction was negative in the few animals tested after infection. *G. gerbillus* was slightly less susceptible to fatal infection than the Eastern cotton rat *Sigmodon hispidus hispidus*. No gerbille of either species was found naturally infected. The animals used in the experiments were trapped in the desert near Cairo where they abound.

John W D Megaw

ZARAFONETIS C J D The Susceptibility of the Rodents, *Gerbillus pyramidum* and *Gerbillus gerbillus* to Experimental Tsutsugamushi Infection (Scrub Typhus) *Proc Soc Exper Biol & Med* 1945 June v 59 No 2, 113-16

Four strains of rickettsiae isolated from scrub-typhus patients in Imphal, Calcutta and Ceylon were transmitted with equal success through series of passages maintained mostly by intraperitoneal inoculation in the two species of gerbilles used in the experiments described in the immediately preceding paper. When large doses of infected peritoneal washings were given by subcutaneous, intraperitoneal, or intravenous injection death invariably resulted in 9-12 days and numerous rickettsiae were found in the abundant peritoneal and pleural exudate. The smears were stained with a 1 per cent solution of methylene blue: this was found more satisfactory for *R. orientalis* than Macchiavello's stain which coloured the organisms blue instead of the fuchsin red tint taken on by other species of rickettsiae.

The gerbilles are regarded as suitable substitutes when white mice are not available.

John W D Megaw

ANDREWES C H, KING H & WALKER J Experimental Chemotherapy of Typhus. Anti-Rickettsial Action of *p*-Sulphonamidobenzamide and Related Compounds. *Proc Roy Soc Ser B* 1946 Jan. 10 v 133 No 870 20-62. [52 refs]

This highly technical paper deals with the chemistry of *p*-sulphonamidobenzamide and many other related compounds with anti-rickettsial activity including no fewer than 13 discovered in the course of the investigation. The biological aspect of the work has already been described in an article by ANDREWES, KING, VAN DEN ENDE and WALKER [see this *Bulletin* 1945 v 42 20]. The present paper will be of special interest only to workers engaged in chemotherapeutical research and these will wish to read it in original.

John W D Megaw

DAVIS W A [U.S.A. Typhus Commission] Typhus at Belsen. 29 mimeographed pp. 4 tables & 1 map [Field Headquarters APO 887 U.S. Army dated 26 July 1945]

This description of the work of the Typhus-Control Unit at Belsen Camp is necessarily a gruesome document. The author who belonged to the U.S.A. Typhus Commission was placed in sole charge of the Unit on April 21 1945. The horrible conditions prevailing in the Camp are now so widely known that no reference to them is needed.

The Unit began its work about five days after contact had been made with the Camp and completed its task on May 25. It dealt solely with preventive measures which consisted almost entirely in the systematic disinfection of the internees with DDT powder and the inoculation with typhus vaccine of the personnel engaged in the work. For most of the time the DDT powder available was of 5 per cent strength: the 10 per cent strength urgently asked for by the author was delayed in arrival.

The degree of overcrowding that prevailed is shown by the fact that in many rooms at least 24 persons were confined in a space approximately 6 ft. wide 12 ft. deep and 8 ft. high: the occupants were not allowed to go out except for a few hours in the afternoon: they lay two in each bunk and on the floor.

May 1946

# *Tropical Diseases Bulletin.*

On the entry of British troops about 45 000 internees were alive in Camp 1 and about 10 000 corpses were still unburied. Among the living there were about 5 000 cases of famine oedema, 3 500 of typhus 20 000 of enteritis and 10 000 of tuberculosis. In Camp 2 there were 16 000 internees. The first task was to bury the dead erect latrines, clear away excrement, establish a water supply and begin the evacuation of the "fit". A large 10-gun power duster was assembled by April 22 and all persons sent to 50 000 persons had been dusted in Camps 1 and 2 and before admission to hospital (11 890) had been bathed and disinfested before admission.

The effect of disinfection was spectacular the last attack of typhus among the internees was on May 14 so that obviously the epidemic had been brought to an abrupt end. This result was strong evidence that transmission had been by living lice rather than by the dried faeces of the insects and it was brought about in spite of failure to achieve 100 per cent. destruction of the lice. Cases continued to occur among the attendants on the sick, but though the patients had been disinfested the possibility of transmission by live lice could not be excluded. Among 98 British medical students who worked at the camp there were six cases of the fever among British workers at Belsen was 8.5

The average duration of the fever among British workers at Belsen was 8.5 days and none of the attacks was severe. The German medical officer in charge of the nurses refused to allow them to be inoculated on the ground that this had already been done but afterwards it was admitted that they had not received any vaccine.

The only group of helpers who remained free from infection were the members of the American Field Service Unit the author seems to suggest that their special immunity was due to their having received the Cox type of vaccine whereas the others had received the Craig type. (In the absence of information regarding the degree of exposure to risk, the time of inoculation, and possible earlier vaccination this suggestion should be received with reserve.)

About 10 persons were disinfested with each pound of powder  
John W D Megees

SILVA, R. & KORCIOWSKA, Léonie Contaminations de laboratoire chez les individus vaccinés dans la typhus exanthématique. [Laboratory Infection with Exanthematic Typhus in Vaccinated Persons.] Bull. Soc. Path. Exot. 1945 v 38 Nos. 11/12 320-23.

A laboratory worker had received nine doses of vaccine at intervals of about seven days. The first seven doses were of murine and the last two of bivalent vaccine. Eight days after the end of the course of vaccination he was attacked by typhus fever of a very mild type. The complement-fixation titre with classical antigen rose to 1-840 and with murine antigen it rose to 1-160 so the diagnosis was classical typhus.

Another worker had received five doses of bivalent vaccine, and nearly five months later he had a very mild attack in which the complement-fixation titre rose to 1-840 with both classical and murine antigen. On the strength of this the diagnosis of "mixed infection" was made.

[The term mixed infection presumably means an infection due to *Rickettsia prowazekii* and *R. mooseri* - if so, most observers would hesitate to regard the complement fixation findings as satisfactory evidence on which to base so inherently improbable a diagnosis especially in the case of a person who had received bivalent vaccination.]  
John W D Megees

Plotz H & Wertman K. Modification of Serological Response to Infection with Murine Typhus by Previous Immunization with Epidemic Typhus Vaccine. *Proc Soc Exper Biol & Med* 1945 June v 59 No 2 248-51

The responses to the complement fixation and rickettsia-agglutination tests are normally very consistent among persons attacked by epidemic (louse borne) and endemic (flea borne) typhus fevers. Much higher titres are observed in tests made with the homologous than in those made with the heterologous antigen. The authors found that among patients who had previously been protected by epidemic typhus vaccine anomalous responses were obtained, as can be seen from the table compiled from three tables illustrating the paper. The first two examples in the table show the kind of responses usually obtained in unvaccinated persons about the end of the third week of attacks of epidemic and murine typhus. The other entries relate to patients suffering from murine typhus who had been vaccinated during the previous two years with the epidemic typhus vaccine used in the U.S.A. Army. The interval since vaccination is shown in brackets.

	Disease	Day of disease	Weil-Felix titre		Complement fixation titre		Rickettsia agglutination titre	
			OX19	OX2	Epid.	Murine	Epid.	Murine
Unvacc.	Epidemic T	19	2,560	80	640	0	5 120	1,280
Unvacc.	Murine T	20	160	0	0	160	640	10 240
Vacc. (2 y)	Murine T	21	2,560	0	640	320	80	1 280
Vacc. (3 m.)	Murine T	22	160	0	1 280	640	320	640
Vacc. (1 m.)	Murine T	21	320	0	160	160	5 120	10 240
Vacc. (3 m.)	Murine T	18	1 280	0	640	160	5 120	10 240
Vacc. (?)	Murine T	15	640	320	80	10	1 280	5 120
Vacc. (2 m.)	Murine T	24	80	40	320	320	1 280	5 120

The anomalous response persisted till late convalescence for example in two patients tested on the 159th and 70th days respectively in both of whom the epidemic complement fixation titre was 1-320 and the murine titre 1-160 though the murine rickettsia-agglutination titres were 1-2,560 and 1-1 280 respectively and the corresponding epidemic titres were 1-320 and 1-160.

No such anomalous reactions were observed in persons suffering from various other diseases due to virus bacterial or protozoal infections so the authors conclude that the unusual reactions are due to previous immunization with rickettsial products followed by infection with murine rickettsiae.

It was observed that previous immunization with epidemic typhus vaccine had little or no effect on the severity of the subsequent attacks of murine typhus.

John W. D. Megaw

Rumreich A. S. & Koepke Jean A. Epidemiological Significance of Seasonal Variations in Rodent-Ectoparasite Distribution. *Pub Health Rep* Wash 1945 Nov 30 v 60 No 48 1421-8 2 figs [18 refs.]

The object of this investigation was to obtain epidemiological evidence of the relative importance of the various potential vectors of endemic typhus. Very large numbers of rats were trapped throughout the year and their ectoparasites were identified and counted. The localities investigated were Jacksonville Florida, Mobile Alabama and Honolulu. The numbers of rats examined in these places were 4 663, 6 123 and 6,382 respectively.

In Jacksonville the prevalence of *Xenopsylla cheopis* and of the mite *Laelaps kansasensis* corresponded to the incidence of endemic typhus when allowance was made for a time lag of one month in the occurrence of the disease. Both parasites were almost equally numerous.

A similar correspondence existed between *X. cheopis* and endemic typhus in Mobile but the correlation with *L. kansasensis* was practically nil. *X. cheopis* was more abundant than the mite in the ratio of 1.7 to 1.0.

The findings in Honolulu were quite different. the prevalence of *X. cheopis* was not correlated with the incidence of the disease and although some correlation occurred in the case of *L. kansasensis* it was not statistically significant. The mite was more abundant than the flea in the ratio of 3.5 to 1.0.

The rat mite *Liponyssus bacoti* which experimentally is a proved vector was found in insignificant numbers in Mobile and Honolulu. it was so erratic and contraseasonal in Jacksonville that it could not have been an important vector. None of the other ectoparasites of the rat could be suspected of being a vector on the evidence obtained.

The imperfections incidental to the survey are discussed, but after giving the fullest weight to these the authors are of opinion that *X. cheopis* may be accepted as at least an important vector in Jacksonville and as the principal vector in Mobile but the available evidence does not support the assumption that this flea plays an equivalent rôle in Honolulu. The mite *L. kansasensis* is dismissed on the ground that it has not been shown to be infectible either in nature or experimentally.

[The findings on which the authors have based their conclusions cannot be abstracted, the whole paper deserves close study by all who contemplate making an investigation of the same kind. a vast amount of highly skilled work has been involved in its production, and few workers can hope to command either the opportunity or the special knowledge needed for carrying out so complete a survey.]

The authors have not referred to the question whether the lack of correlation between the prevalence of *X. cheopis* and typhus fever in Honolulu is actually opposed to the assumption that the flea is the principal or sole vector in the area. It may be impossible to give an answer to this question because, if a vector were present in numbers sufficient to maintain transmission the prevalence of the disease might well depend on other factors as well as on the density of population of the vector.]

John W. D. Meyer

TATTERALL, R. N. & PARRY, T. E. An Outbreak of Typhus Fever (O\K) in India. *Indian Med. Gaz.* 1945 Sept. v. 80 No. 9 433-7 2 figs. on 1 pl., 2 text figs. & 4 charts.

This report deals with 121 cases of "typhus fever (O\K)" occurring in a British regiment during October and November 1943 in an area "adjacent to Burma."

The regiment went into camp in the affected area on October 11, 1943 and remained till November 2. The first case occurred 9 days after arrival, and the last 17 days after departure from the area.

Some of the chief clinical features were as follows (the figures in brackets show percentage incidence) —frontal headache with photophobia (100) sore throat (83) eschar (9) a rash was seen in 79 cases it was macular in 39 and papular in 40 generalized adenitis (85) mental apathy (99) sometimes amounting to coma cyanosis and flushing (85) chest signs (88) conjunctival injection (69) deafness (33) and secondary fever (17).

The Weil-Felix (O\K) titre usually reached 1-200 by the 13th day. The maximum readings were obtained between the 13th and 22nd days and after

this the titre tended to fall. The Dreyer technique and standard army suspensions were used. The average leucocyte count in the second week was 5 400 per cmm. The average differential count was polymorphonuclears 47 per cent lymphocytes 46 per cent and monocytes 6 per cent. Eosinophilia was common in the 4th and 5th weeks. There were 11 deaths. A poor response to the exercise tolerance test persisted for three to four weeks [presumably after defervescence].

Post mortem examinations were made in all the fatal cases. The right side of the heart was dilated in ten there was extreme pulmonary congestion in ten pneumonia in six enlarged mesenteric glands in all congestion of the meninges and surface of the brain in all and petechial haemorrhages in the stomach ileum caecum or colon in five.

John W D Megaw

GRIFITHS J T Jr A Scrub Typhus (*Tsutsugamushi*) Outbreak in Dutch New Guinea. *J Parasitology* 1945 Oct v 31 No 5 341-50 5 figs

In this outbreak there were 931 cases with 34 deaths among U.S.A. troops who landed on July 30 1944 on a coast in the Vogelkop Peninsula of Dutch New Guinea.

More than 500 of the cases were contracted in semi-cleared areas covered with knee-high grass growing on moist soil there were also scattered cocoanut banana papaya and kapok trees remains of village sites small plantations and native gardens.

The incidence was low (26 cases) in two islands covered with cocoanut trees among which a dense undergrowth had sprung up so that only small amounts of grass and scrubby growth remained. The scantiness of the grass was suspected of being the cause of the smallness of the mite population.

Another area consisted of a strip of grass and ground-clinging vines along the beach backed by forest from this environment there were 90 cases but the incidence was low compared with that in the first area. Most of the military base consisted of dense forest where no grass grew in this area no cases occurred though scrub itch was common.

The incubation period was 7-17 days the outbreak rapidly reached its height by August 15 about this time an average of 45 cases was being admitted daily but soon a rapid decline set in by the middle of September the daily admissions had fallen to three or four and at the end of the month an average only of one case daily was occurring.

The removal of grass and undergrowth from a site was found an effective method of control when the top soil had dried out the area was considered safe. There was no evidence that rat control was of any practical value. Impregnation of clothing with a soap emulsion containing dimethyl phthalate was strikingly successful.

Some of the clinical features observed in a sample group of 275 patients were as follows (the figures show percentage incidence) eschar with local lymphadenitis (92) photophobia (45) insomnia (75) generalized lymphadenopathy (95) and measly rash on body and limbs (28). The commoner sites of the eschar were the axillary region (24) scrotum (20) thighs (11) inguinal region (8) and penis (8). The temperature usually fell by lysis (70) when it fell by crisis (30) the attacks were much less severe on the whole and the convalescence was more rapid.

Of the 34 deaths in the whole outbreak (3.65 per cent.) 18 occurred on the 11th to 14th day 10 on the 15th to 18th day and 6 on the 20th to 26th day from the onset.

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John W D Megaw

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May 1946

## Tropical Diseases Bulletin

DESIMON M D Clinical Picture of Scrub Typhus in East African Troops on the Burma Front. *East African Med J* 1945 Nov v 22 No 11 360-67

During the last quarters of 1944 615 cases were treated in a General Hospital for East African troops in Burma. The author describes some features of the disease as seen in 200 cases selected for their severity and interesting complications. The incubation period was two to three weeks.

Generalized lymphadenitis was usual. A primary sore was seen in 35 cases and a rash, usually inconspicuous and macular in 15. Nearly all the patients complained of pains in the bones and joints. Eight patients became insane two of them appeared unlikely to recover and one having cut his abdomen open with a razor blade ripped off the intestines from the mesentery.

Various types of neuritis occurred affecting the auditory nerve in eight cases, the facial in two the laryngeal in two the optic in one nerves of the legs in six, and of the arms in one. Abscesses after injections were common there was phlebitis of the femoral vein in two cases, and suppurative peritonitis in one. Of the 615 patients 12 died nine of these had been evacuated between the 6th and 11th days when transfers after the 4th day were forbidden the fatality rate became negligible.

The naked-eye post-mortem findings were uniform and rather disappointing the lungs were congested the heart was flabby but normal in size the spleen was enlarged, soft and friable the kidneys were congested the mesenteric glands were enlarged there were usually pinpoint haemorrhages in the stomach and intestines and there was congestion of the superficial vessels of the brain. The microscopic findings were endothelial swelling and proliferation in the capillaries of the brain but no perivascular aggregation of cells was seen the cells of the renal tubules were swollen and necrosed and there was endothelial proliferation in the lymph glands.

The Weil-Felix reaction (*Proteus OXK*) was of the usual type.  
John W D Vogan

SOKOLOFF M & GARLAND L H Cardiovascular Disturbances in Typhusgammahl Disease. *C.S. War Med Bull* 1945 Dec. v 45 No 6 1054-68, 5 figs. [14 refs.]

The after effects of scrub typhus on the cardiovascular system were studied in 35 convalescent patients at an average interval of 4.7 months after the onset of the attack. All the patients had been ambulatory for at least six to eight weeks, many of the findings cannot be estimated because there was no information to show what proportion of the total number of convalescents was represented by the patients. It was thought possible that the 35 men formed a relatively small percentage of the total. [Apparently they had been sent for special observation and treatment.]

The special symptoms were weakness, dyspnoea, palpitation of varying degree and precordial pains. Electrocardiograms showed no gross abnormalities in any case but minor defects were found in seven cases. There was no evidence of definite cardiac enlargement in four patients of whom one had appreciable enlargement of the left ventricle. In 14 of the patients roentgen-kymograms showed abnormal contractions affecting the left ventricle in all but one of them.

Decrease in the vital capacity was seldom pronounced, but 75 per cent. of the patients could not hold their breath for the normal time of 45 seconds, and in seven cases the maximum time was only 20 seconds.

Two-thirds of the men had tachycardia on standing and nearly half of them had abnormally high pulse rates after mild exercise tests. About 75 per cent had dyspnoea, palpitation fatigue and dizziness after the standard exercise tolerance test.

All the evidence went to show that the defects were due to scrub typhus because a group of men who had been exposed to malaria dysentery and other adverse conditions to the same degree were found free from these defects. The pathogenesis of the condition is discussed. It is left an open question whether the chief factor was myocarditis peripheral vaso-motor instability or perhaps lesions of the cerebral vaso-motor centres.

Progressive improvement resulted from treatment. The conclusion reached is that convalescence in many cases of tsutsugamushi disease is protracted and that disabling circulatory disturbances may persist in some cases up to at least six months from the onset.

John W D Megaw

MURRAY E S ZARAFONETIS C J D & SNYDER, J C Further Report on Effect of Para-Aminobenzoic Acid in Experimental Tsutsugamushi Disease (Scrub Typhus) *Proc Soc Exper Biol & Med* 1945 Oct., v 60 No 1 80-84

Experiments are described which demonstrate that para aminobenzoic acid can greatly reduce the fatality rate among gerbils inoculated with lethal doses of *Rickettsia orientalis*. The sodium salt (NaPAB) was used and was given by a combined method—orally with food starting a few hours after intraperitoneal inoculation with the rickettsiae and also subcutaneously starting on the 4th or 5th day after inoculation.

The results obtained in the whole series of experiments were that among 130 control animals only two (1.5 per cent) survived whereas among 128 treated animals 105 (82 per cent) survived. Most of the animals received 10-1000 certainly lethal doses of rickettsiae and very few of the animals that died in spite of treatment showed the typical lesions of the disease at autopsy. The strains of rickettsiae used in the trials originated from Calcutta Ceylon Imphal and New Guinea.

Details of the preparation of NaPAB and of the method of administration are given in the paper.

John W D Megaw

SNYDER, J C & ZARAFONETIS C J D Effects of Para-aminobenzoic Acid in Experimental Tsutsugamushi Disease (Scrub Typhus) *Proc Soc Exper Biol & Med* 1945 Oct., v 60 No 1 115-17

This paper contains a description of experiments carried out before those referred to in the preceding abstract. PABA was given mixed with the food to gerbils after intraperitoneal injections of 100 to 1000 lethal doses of *Rickettsia orientalis* but the only result was a slight prolongation of the survival time.

The early experiments on the combined oral and parenteral treatment with sodium salt of PABA (NaPAB) are also described in these the survival rates after 10-100 lethal doses of the Ceylon strain were 87½ and 62½ per cent respectively.

John W D Megaw

ROSE H M DUANE R B & FISCHER E E. The Treatment of Spotted Fever with Para-Aminobenzoic Acid. *J Amer Med Ass* 1945 Dec. 22 v 129 No 17 1160-61 1 chart.

Para aminobenzoic acid (paba) has already been found effective in the treatment of louse-borne typhus in man by LEOMANS and his colleagues [see this

tested in the following way — A group of 50 Swiss mice received three doses each of 0.25 ml. intraperitoneally at weekly intervals. Ten days after the last dose they and 50 unvaccinated mice, were challenged, in groups of eight, with intraperitoneal injections of spleen substance from infected mice. The dose of infected material was graduated by dilution in ten-fold steps from  $10^{-1}$  to  $10^{-8}$ . The numbers of mice dying within 25 days after being challenged are shown. The infecting doses are arranged in descending series, beginning from the left —

Vaccinated	5	3	2	1	3	0
Controls	8	8	7	8	6	4

After vaccination by the subcutaneous route with similar doses, the comparable figures for four groups of 10 mice each were as follows —

Vaccinated	7	6	2	5
Controls	10	9	8	4

The significance of the results is discussed. It is admitted that the vaccine seems to give poor protection compared with the results obtained in mice protected against epidemic typhus by epidemic type vaccine but in view of the intense susceptibility of the mouse to scrub typhus it was thought that this impression might be misleading as epidemic and scrub typhus in man are so similar in their clinical features, there seems some reason to hope that the vaccine against the latter may prove as effective as the epidemic type vaccine.

The doses which have been suggested for trial in human beings are three of 1.0 ml. each given at weekly intervals and a "booster" dose of 1.0 ml. every three months.

The authors finally point out that without a field trial, it is impossible to decide whether this vaccine will be of any value in man.

*John W. D. Megee*

BUCKLAND F. E., DUDGEON A., EDWARD D. G. H., HENDERSON BEGG A., MACCALLUM F. O., NIVEN J. S. F., ROWLANDS, L. W. & VAN DEN ENDE, M. with H. E. BARGMAN, E. E. CURTIS & M. A. SHEPHERD. Scrub-Typhus Vaccine. Large-Scale Production. *Lancet* 1945 Dec. 8 734-7  
8 figs.

The authors tell the remarkable story of "Special Operational Store-Tyburn," which was organized for the large-scale preparation of scrub-typhus vaccine on the lines described in the immediately preceding paper with the object of carrying out field trials in the Far-Eastern war zone.

A large laboratory was designed and constructed at Frant in Sussex. Housing for the breeding colonies of cotton rats was ready within 31 days and the complete laboratory was opened on May 31 1945 within 109 days of the decision to start the operation. This feat was made possible by the military priority accorded to the scheme.

All the rooms in which there was risk of infection were ventilated on the plenum system and were fitted with apparatus for the aerosol-spray treatment of the air with lactic acid. Air from the special inoculating and grinding cabinets was extracted and passed through an electric furnace on the roof to prevent the discharge of infected particles into the open air. Details are given of the elaborate precautions against infection of the workers and among 60 persons employed only three were attacked by the disease. One person was suspected of having inhaled infected droplets while transferring material with a Pasteur pipette another had a skin trauma caused by a broken pipette containing infected material and the third had been washing unsterilized infected Petri dishes. All three made uneventful recoveries. They and the rest of the staff had been vaccinated.

The scheme was planned on the basis of importation from the U.S.A. of 5 000 cotton rats monthly this with local breeding was expected to provide 12 000 rats monthly. These rates were not attained altogether 19,223 rats were imported and 10 836 were bred up to the time of writing 16,882 had been used but about 20 per cent were discarded because of death before the fourth day or insufficient rickettsial yield. During the five and a half months ending September 30 201.9 litres of vaccine were prepared.

When the war against Japan came to an end the operation ceased to be urgent but it was continued till the available rats were used and by October 31 when 300 litres of vaccine had been prepared it came to an end.

The preparation of the vaccine was on the lines described in the preceding paper but a few modifications were introduced. The mice used for preparing infecting suspensions were given sulphathiazole in a concentration of 1.0 per cent in a cubed diet instead of by intraperitoneal injection. Smears were stained by alkaline polychromed methylene blue after heat fixation and treatment with  $\text{N}/1$  HCL.

Altogether 15 100 mice were used to prepare the seed suspensions but of these 9 163 died or were discarded because of gross contamination. Each batch of vaccine was tested by rickettsial counts and complement fixation tests it appeared that the antigenic content was correlated with the rickettsial count though difficulties were encountered with the staining technique and probably the true counts were much higher than those actually observed. Several interesting pieces of research were carried out including further attempts with unsatisfactory results to cultivate the organisms by the yolk-sac method. Filtration experiments suggested that the size of *Rickettsia tsutsugamushi* corresponded closely with that of *R. prowazeki*. Attempts at serial passage through the lungs of sheep and goats failed.

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John W. D. Megaw

## YELLOW FEVER.

LAURET F. Jr. La situación de la fiebre amarilla en Venezuela. [Yellow Fever in Venezuela.] *Bol. Oficina Sanitaria Panamericana* 1945 Sept 24 No 9 778-83 3 maps English summary

During 1929 an outbreak of jungle fever occurred in the Cuyuni Valley a sparsely settled wild region in Venezuela. This proved to be autochthonous as the settlements where the fever occurred are located at considerable distances from places where long before cases had been reported. Since the creation of the National Service for the Prevention of Yellow Fever in Venezuela in 1937 the yellow fever problem has been studied with great care continuously. There are 78 viscerotomy posts in operation where positive protection tests have been made. This organization has made it possible to locate another yellow fever area, as shown in one of the attached maps. During the 1929 outbreak in Cuyuni 11 cases occurred among laborers working in sawmills and other cases were reported in workers clearing timber areas and junglelands where the *Haemagogus* vector prevails. An *Aedes taeniorhynchus* or long-sleeve monkey caught in the San Camilo Forest showed a positive reaction to the disease. In brief there are in Venezuela two endemic jungle yellow fever areas both located in the basins of Maracaibo Lake and the

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Orinoco River. The first where the 1944-1945 outbreak centred, lies in the so-called Venezuelan Guayana, bounded by the Caroní river and the borders of the State of Bolívar with Brazil and British Guayana. The second is in the States of Táchira and Barinas its principal focus being in the so-called San Camilo Forest on the transitional area between the Andes Mountains and the Apure and Barinas plains. There may perhaps be another yellow fever focus at the northern watershed of the Andes towards Maracaibo Lake although up to the present time only one case has been reported.

KAPLAN M. & GLUCK, A. C. Méningo-encéphalite après vaccination anti-amarile. [Meningo-encephalitis after Vaccination against Yellow Fever] *Bull et Mem Soc Méd Hôp. de Paris*. 1945 No. 26/31 574-6.

The record of the clinical symptoms of a 4½-year-old child who became ill 5 days after being vaccinated, by the scarification method, with a neurotropic strain of yellow fever virus supplied by the Pasteur Institute at Dakar. This child developed typical meningeal symptoms about the 11th day after vaccination, with high fever headache somnolence, a convulsive crisis and a state bordering on coma. Lumbar puncture produced a clear aseptic fluid and showed a mononuclear hypercytosis. After two or three days there was sudden improvement and the patient made a complete recovery.

Attempts to isolate yellow fever virus from the cerebrospinal fluid by intracerebral inoculation of mice gave inconclusive results, but protection tests with the same fluid were positive. The authors are of the opinion that in order to avoid such accidents it is preferable to use inactive tissue culture virus for vaccination.

E Hindle

## DENGUE AND SANDFLY FEVER

FLORIO L., STEWART Mabel O. & McGRACE, E. R. The Etiology of Colorado Tick Fever. *J Exper Med* 1946 Jan. 1 v. 83 No 1 1-10 8 figs.

The authors, continuing their work on Colorado tick fever [this Bulletin 1945 v. 42, 118] now report experiments on the filterability of the causal agent. Two strains were maintained by passage through hamsters, and serum from infected animals was used as the source of virus in filtration experiments. Hamsters were injected intraperitoneally with test filtrates, and lowering of the white blood count was taken as the criterion of successful infection. Both strains of virus were found to pass through 262 and 181µm collodion membranes. In seven experiments with filtrates of 24µm membranes two groups of hamsters showed clear-cut evidence of infection and the presence of the virus was demonstrated by passage in three other groups. A human volunteer developed Colorado tick fever following subcutaneous injection of infected hamster serum filtered through a 181µm membrane. Similar experiments with the filtrate of a 24µm membrane proved negative.

The authors conclude that the infectious agent of Colorado tick fever passes through 24µm membranes and should be classified as a virus.

A J Rhodes.

## PLAGUE

GIRARD G Hémoculture et bactériémie dans l'infection pesteuse [Culture and Bacteraemia in Plague.] *Bull Soc Path Exot* 1944 v 37 Nos 11/12 328-31

An original question whether a flea can become infected when fed on a case in which blood culture has proved negative resolves itself for the author into two further questions —(1) How many organisms in a blood culture are necessary to initiate a plague culture? and (2) Are there any bactericidal or inhibitory substances carried over with the blood in a blood culture which would be sufficient to render non-viable a proportion of the organisms present? The media used for which the author expresses decided preference were one in which the peptone was Chapoteaut's peptic peptone and the other called Uclaf in which the peptone is a tryptic digest of foetal tissue to which gluten is added. In his experiments using dilutions of a suspension containing about 20 million bacteria per cc the author arrives at the conclusion that growth of the plague bacillus can be initiated in a suitable medium when the inoculum contains no more than a single living organism. This conclusion seems to provide the answer to the first of the two questions posed. The second question is dealt with firstly by showing that the addition of any blood to any nutrient medium will act favourably in the initiation of growth of the plague bacillus and secondly by showing that the addition of any blood of any animal whether a normal animal which has been used to furnish plague serum (antitoxic not bactericidal) is immaterial so far as relates to any but a favourable effect on the growth of the plague bacillus. And thus the final conclusion may be reached that if a blood culture proves negative it is because that blood contains no viable organisms and that therefore no flea could become infected by ingestion of that blood. The blood of a plague case too contains no bactericidal or inhibitory substances which could complicate growth conditions.

W F Harvey

## CHOLERA.

SOMAN D W & NAIR S K Sub-Types of Cholera Vibrio Isolated from Cholera Patients in Bombay *Indian Med Gaz* 1945 Oct. v 80 No 10 512-14

A survey of the conditions in town or district during the prevalence of disease has great importance for epidemiology by presenting data for future comparisons and predictions. Such data in India are few and non-existent in Bombay. The authors have seized the opportunity of epidemic cholera during 1943 and 1945 in Bombay City to obtain and publish these data. They refer to the serological sub-types Inaba and Ogawa cholera vibrios of sub-group I. As the authors mention (and this is one aspect of the value of this Bombay survey)— Investigations carried out over a period of years in the Madras Presidency have shown extensions and recessions of the area in which the respective sub-types may be the form associated with outbreaks. Their findings given as a summary were: The prevalent and predominant sub-types of cholera vibrio have been determined. One hundred and sixty four strains isolated have been tested against cholera O serum group I and Inaba and Ogawa specific sub-type sera. One hundred and sixty-one strains belonged to the Ogawa subtype the remaining three strains were found to be Inaba sub-type. No intermediate type was recorded.

W F Harvey



UNITED STATES NAV MED BULL. 1945 Dec. v 45 No 6 1049-53 Report on Cholera Studies in Calcutta, Value of Chemotherapy in the Treatment of Cholera and use of Blood Plasma in Cholera Collapse. Epidemiology Unit No. 50. [AMBERSON J M.]

The object of this report is to show the value of chemotherapy in general it is not an analysis of the relative value of specific medicaments. A comparative series of trials was set up which contrasted no treatment other than the usual supportive treatment with chemotherapy which, of course, involved throughout also the usual supportive treatment. Very special consideration is paid to the use of blood plasma as supportive treatment along with chemotherapy. There was a total of 372 cases of clinical cholera available for analysis.

The groups in this report are set out as (A) 3 gm sulphaguanidine every 4 hours for 3 days and twice daily for the next 3 days to a total of 72 gm. (B) Supportive treatment only represented by intravenous hypertonic and normal saline solution together with oral stimulants to offset dehydration emaciation and circulatory failure. This group of patients the control group received inert substance (3 gm. calcium carbonate every 4 hours for 3 days) (C) One gm. sulphadiazine every 4 hours for the first day and 2 gm. every 4 hours for the following 2 days to a total of 30 gm. (D) Penicillin intramuscularly in normal salt solution the initial dose being 100 000 units with 25 000 units every 4 hours thereafter to a total of 200 000 units. (E) Received the combined treatments of C and D. Positive value is accorded to chemotherapy and in the matter of data particular stress is laid on the combination of supportive blood plasma with any or all of the chemotherapeutic groups. These data are set out in tabular form —

	Plasma plus chemotherapy	Chemotherapy alone	Control
Lived	35	274	37
Died	0	3	23
Death Rate	0%	1 1/2%	38 3%

There can be little doubt of the value of chemotherapy in cholera.

W F Harvey

## BACILLARY DYSENTERY

SMITH L A. Shiga Dysentery *J Amer Med Ass* 1946 Jan. 5 v 130 No 1 18-22.

By "Shiga dysentery" the author means that due to any organism of the *Shigella* group in short bacillary dysentery. Mild attacks of diarrhoea or of dysentery [referred to by British troops as the squitters or Gippy tummy] are known to American troops as the G.I.s. The early diagnosis of bacillary dysentery on clinical grounds, by macroscopical examination of the stools, or by culture of the stools, may be misleading and is often impossible. Proctoscopy in the knee-elbow position is quite easy in a patient with diarrhoea, if performed after a natural motion and without enema clearance. This technique affords the earliest possible positive diagnosis of bacillary dysentery and on repetition shows the progress of the disease. The findings indicate three phases of development of the bowel lesions in bacillary dysentery viz —

(1) The *Early Phase* is to be seen within a few hours of the onset of symptoms the essential features are oedema and generalized hyperaemia of varying intensity of the mucosa. There may be miliary mucosal abscesses of pin point to pin head size initially these are creamy in colour and are due to localized accumulation of leucocytes later they are topped by shallow ulceration. In severe cases there may be superficial necrosis of the mucosa with the formation of a pseudo-membrane this on being stripped off leaves a red or purple raw surface which bleeds easily.

Efficient early treatment of bacillary dysentery in this stage causes rapid regression of the bowel lesions.

(2) The *Middle Phase* is characterized by granulations indicative of healing and by ulceration. The granulations vary in number and size are dusky red or purple in colour and are irregular in shape there may be central ulcers in them. These ulcers are from 0.5 mm. to over 1 cm. in diameter and are round oval or serpiginous their bases are grey and dirty. The proximal surfaces of the valves of Houston are a usual site for these lesions and a patient with much tenesmus will have many of them in the lower 6 cm. of the bowel. As healing progresses granulation fills in the ulcers the colour of the new tissue lightens and eventually the normal vascular pattern of the mucosa is restored perhaps many days after the patient is symptom free.

Efficient treatment of the dysentery at this stage is much more slowly effective in causing regression of the bowel lesions.

(3) The *Late Phase* is seen in severe untreated cases of bacillary dysentery where indolent ulceration persists for long and heals slowly often with extensive superficial scarring.

After discussing the differential diagnosis of bacillary dysentery and reaffirming that in 90 per cent. of cases early proctoscopy yields the diagnosis the author reviews the response to treatment of his cases symptomatically objectively and in relation to the reversal of the cultural findings in the stools. Previously clinical response and the time taken to obtain it have been the criteria of success of treatment but these are misleading unless proctoscopic examinations are made. Four groups of cases were treated respectively — (1) without chemotherapy (2) with sulphaguanidine—4 gm. three-hourly for four doses and then 2 gm. four-hourly—a total of 48 gm. in 72 hours (3) with sulphadiazine (given with equal weights of sodium bicarbonate) 4 gm. initially then 2 gm. four-hourly for four doses then 1 gm. four hourly for four doses and then 1 gm. six-hourly for seven doses—a total of 23 gm. in 72 hours and (4) by combined sulphaguanidine and sulphadiazine therapy (sulphadiazine as outlined for three days on the third day sulphaguanidine as outlined this being continued until the fifth day).

The author concludes that the best period for effective treatment is in the first twenty four hours of the disease. Sulphadiazine at this time causes prompt cessation of the symptoms and signs but the mucosal lesions may not disappear until some time after this especially if treatment has been delayed. Sulphadiazine appeared to be more rapid in its action than sulphaguanidine and caused the stools to become negative on culture within 24 to 36 hours.

A R D Adams

MAJUMDER A R, BAGCHI A K & GHOSH B K. Sulphanthyl Benzamide in the Treatment of Bacillary Dysentery (A Preliminary Note.) *Indian Med Gaz* 1945 Oct. v 80 No 10 500-501

Sulphanthyl benzamide was tried in 19 cases of bacillary dysentery. cultures had been made in 14 of the cases but in only 4 were pathological organisms isolated—Sonne in 3 and Flexner in 1. The dosage was 2 tablets three

REDDY D G & RANGAM, C. M. Jaundice in Amoebic Liver Abscess. A Report of Two Cases. *Indian Med Gaz.* 1945 Oct. v 80 No 10 501-2, 4 figs. on 1 pl.

Two cases of amoebic abscess of the liver diagnosed at post mortem examination are described in one case a single abscess had ruptured into the peritoneal cavity while in the other case there were three abscesses in the right lobe of the liver but none had ruptured, though a diffuse peritonitis was present. Amoebae were found in the walls of the abscesses in both cases. Both patients were jaundiced in one case the abscess pressed on the right hepatic duct while in the other case the common bile duct was blocked. *J F Corson*

GILJE, L. E. & LAMPSON, R. S. Acute Appendicitis in Amoebic Dysentery Report of a Case. *U.S. Nav Med. Bull* 1946, Jan. v 48 No. 1 109-11

KNOLL, Elta W & HOWELL Katharine M. Studies on *Dientamoeba fragilis* its Incidence and possible Pathogenicity *Amer J Clin. Path.* 1945 May v 15 No 5 178-83. [19 refs.]

In discussing *Dientamoeba fragilis* the authors note that the various surveys in which it has been identified indicate that its distribution is widespread throughout the world. If laboratory workers were experienced in the identification of this parasite they would find that its incidence in any population is probably as high as or even higher than that of *E. histolytica*. As regards its possible pathogenicity a series of cases is described in children and adults in which it appeared to be the only organism present, apart from non-pathogenic bacteria. The symptoms in these cases were abdominal discomfort and pain bouts of diarrhoea, nausea and vomiting and some fever. During the attacks *D. fragilis* in very large numbers appeared in the stools. In some of the cases symptoms had persisted for two or more years. In all these cases the symptoms ceased under carbarsone therapy while *D. fragilis* disappeared from the stools. As a result of their studies the authors conclude that *D. fragilis* can be pathogenic to man. Attempts to discover the organism in dogs cats and rats met with no success while repeated administration of rich cultures to kittens *per os* and *per rectum* failed to bring about an infection. *C M Wenyon*

DÍAZ ATELES A. A Study of *Balantidium coli*. Report of Two Cases in Children successfully treated with Stovarsol. *Puerto Rico J Pub Health & Trop Med.* 1943 Mar v 18 No 3 287-89 [Refs. in footnotes.] [Spanish version 300-313.]

The author in reviewing recent literature gives an account of two cases of *Balantidium coli* infection in boys nine years of age both of whom had been in intimate contact with pigs. The persistence of the infection for six weeks was established by repeated stool examinations before treatment with stovarsol was instituted. In one case response to treatment was immediate the stools being negative after 48 hours but treatment was continued for a week. In the other case there was no response for three weeks. With increased dosage (750 mgm. daily) the stools became consistently negative. In both cases, a year after cessation of treatment the stools were still negative. Two other children are referred to they were associates of the others but treatment was not carried out as the infection from which they both suffered, was only of a transient nature. *C M Wenyon*

HUMPHREY A. A. *Isospora hominis* Infection in Man. *J Amer Med Ass* 1946 Jan 19 \ 130 No 3 143-5 1 fig

Three cases of *Isospora hominis* infection are described in men who had served in Okinawa and were evacuated to Guam for hospital treatment in July 1945. All three suffered from abdominal discomfort or diarrhoea. The longest period during which oocysts were observed in the stools was during 15 days hospitalization. In all three cases there was some degree of eosinophilia.

C M Wenyon

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

GREAVES F C, GEZON H M & ALSTON W F. Studies on Louse Borne Relapsing Fever in Tunisia. *U.S. Nav Med Bull* 1945 Dec. v 45 No 6 1029-48 9 figs [49 refs]

A general account with special reference to the treatment and control of louse-borne relapsing fever due to *Spirochaeta berberis* in Tunisia.

Since the outbreak of 164 cases in Tunis during 1912 there were only sporadic cases until July 1943 when a major epidemic began which was still in progress during 1945. In 1943 only 6 cases were recorded but in 1944 the monthly cases rose from 8 in January to 4 451 in December and continued to rise in 1945 to 6 536 in March. The total for 1944 was 18 534 and for the first 4 months of 1945 reached 23,221 cases. These statistics are considered by the public health authorities to involve only one-fifth of the actual numbers for the majority of the Arab population seem to prefer not to attend for medical treatment.

The mortality rate showed marked differences. In one small village 80 untreated cases had a mortality rate of 1.25 per cent whilst in another very similar village 71 untreated cases showed a rate of 46.5 per cent among 3 806 cases treated in the Ernest Conseil Hospital in Tunis the rate was 5.46 per cent. There is no satisfactory explanation for these differences and it is possible that other diseases such as typhus typhoid, or plague may have complicated the relapsing fever.

The clinical symptoms were typical but 10 per cent. of 112 untreated cases had no relapses. 62.5 per cent. showed only one relapse and 22.3 per cent. two relapses whilst occasional cases showed three four or five relapses. Laboratory studies were made on 40 patients. The most constant finding was a complete absence of eosinophils in all patients even after the clinical termination of illness.

Penicillin was used for the treatment of 27 patients the total dose being 480 000 units for adults and 360 000 for children. In most cases the spirochaetes disappeared within 24 hours and none was ever found after 48 hours. All these patients showed a rapid clinical recovery and none had a relapse. The results with neosarsphenamine were also equally satisfactory and since this is cheaper and easier to administer it is the drug of choice except when relapsing fever is accompanied by jaundice.

Three guinea-pigs and 27 mice were inoculated with infective material but only in the case of one guinea-pig and 21 mice receiving large doses of heavily infected blood were spirochaetes recovered and then only in the first 24 hours. It is evident that these animals are unsuitable for the isolation of this spirochaete directly from human blood.

Experiments were made on the control of the epidemic in an isolated Arab village by the use of 10 per cent DDT applied by dusting each member of the

household and the bedding and extra clothing. The disease completely disappeared within a fortnight after this treatment and neither lice nor nits were found on 75 people examined in the village 10 days later. Another experiment was made in Ferryville. In the treated area 78.7 per cent. of 851 persons were dusted with DDT in the adjoining control area there were 1 438 persons. The results are shown in the following table —

*Incidence of relapsing fever in the Bellevue quarter of Ferryville May 1945.*

		Total	No deloused	Percent deloused	No huts	No sick	Percent sick	No. with Positive Blood Smears
May 5-12	DDT	851	653	76.7	147	46	31.1	14
	Control	1 438	none	0.0	129	47	36.4	12
May 17-19	DDT					2	0.23	1
	Control					41	2.85	12
May 28-28	DDT					4	0.46	1
	Control					24	1.67	8

It would seem, therefore, that one application of 10 per cent. DDT powder if thoroughly applied to a population is almost completely effective in stopping a louse-borne epidemic of relapsing fever.

E Hinde

LOFGREN, Ruth & SOULE, M. H. The structure of *Spirochaeta mors* as revealed by the Electron Microscope. *J Bacteriology* 1945 Dec v 50 No. 6 679-80 8 figs.

RICHARDSON, A. P. WALKER, H. A. LOBE, Prudence & MILLER, I. The Experimental Basis for the Quantitative Chemotherapy of *B. mors* in Mice with a Comparison of Action of Penicillin and Dichlorophenarsine Hydrochloride. *J Pharm & Exper Therap* 1945 Sept., v 85 No. 1 23-35 2 figs. [10 refs.]

The authors describe detailed experimental procedures for quantitative chemotherapeutic experiments with mice infected with *Spirochaeta mors*. They first show that the number of spirochaetes injected has a considerable effect on the course of untreated infections. Also that the degree of anaemia which develops is roughly proportional to the number of organisms in the peripheral blood.

Five samples of penicillin were tested for their action on the spirochaetes, viz. crystalline sodium penicillin G, commercial sodium penicillin Squibb, pilot plant lot No 860 containing almost no penicillin G, commercial calcium penicillin Squibb, probably a mixture of G and other penicillins, and methyl ester of penicillin G. The activity of these five compounds was compared with dichlorophenarsine hydrochloride in three types of experiments, viz., frequent subcutaneous injections, single daily injections or given by mouth. On the basis of Oxford units, no significant differences were found between the first four samples of penicillin irrespective of the method of administration. The methyl ester of penicillin G was found to be equal to free penicillin G when injected, but had less than one-twentieth of that activity when given orally.

When administered by frequent subcutaneous injections dichlorphenarsine hydrochloride is weight for weight equal to crystalline sodium penicillin G in its activity against *Spirochaeta novyi*  
E Hindle

NAJERA ANGULO L. Receptividad de los murciélagos cavernícolas españoles (*Myotis myotis*, *Rhinolophus euryale* y *Myotis hipposideros minimus*) al virus de la fiebre recurrente mediterránea [The Susceptibility of Spanish Cave-dwelling Bats to the Spirochaete of Mediterranean Relapsing Fever] Reprinted from *Boletín de la Real Soc Española Hist Nat Madrid* 1945 v 43 217-28 1 map

The relationship between *Spirochaeta hispanica* and the spirochaetes causing relapsing fever in Portugal and in Greece (*Sp. hispanica* var *peloponnesica* of Caminopetros) is of considerable interest the author calls the fever caused by these organisms Mediterranean relapsing fever. As biological reactions are important aids in the identification of spirochaetes of apparently identical morphology, he made experiments in 1939 to test the susceptibility of some cave-dwelling bats to infection with *Sp. hispanica*.

These bats were difficult to keep alive and it was found best to keep them at a temperature of 18°C and in an atmosphere of a humidity approaching saturation to get a short incubation period they were inoculated intraperitoneally with blood of guinea-pigs heavily infected with *Sp. hispanica* and those which survived for 4 days or more were examined post mortem.

The results are shown in notes and tables four species were found susceptible namely *Myotis myotis*, *Rhinolophus euryale* and *Rhinolophus hipposideros minimus*. One of these bats *Myotis myotis* is a host of *Schizotrypanum vespertilionis*  
J F Corson

YAKOUB R. Relapsing Fever in Egypt. *J Roy Egyptian Med Ass* 1945 July v 28 No 7 327-30

TAFT W C & PIKE J B Relapsing Fever Report of a Sporadic Outbreak including Treatment with Penicillin. *J Amer Med Ass* 1945 Dec. 8 v 129 No 15 1002-5

A study of eleven cases of relapsing fever observed and treated at an army hospital in Texas during August and September 1944 and April and May 1945. All the patients shortly before admission had camped in a bivouac area where many *Ornithodoros turicata* were present later it was shown that spirochaetal infection was present in the ticks.

The clinical diagnosis of the disease in the initial stages was found to be difficult it was established by dark field examination or stained smear of the peripheral blood. Spirochaetes were found in the blood only during the febrile period when the temperature was above 102°F. Five of the patients developed a skin eruption having the appearance of erythema multiforme which persisted for 24 to 48 hours. A biopsy was made of one of these skin lesions and spirochaetes were found in the superficial layers of the dermis even during the afebrile period. [This interesting observation seems to be the first record of relapsing fever spirochaetes being found in this site.]

Significant neurological manifestations developed in five of the patients even suggesting a diagnosis of meningitis. Spirochaetes were never found in the spinal fluid however either by direct examination or mouse inoculation. Treatment with oxophenarsine hydrochloride administered intravenously with or without bismuth gave disappointing results for although it shortened the attack it did not prevent relapses. In two patients penicillin was given—40 000 units every three hours for 60 doses a total of 2,400 000 units. Both

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were afebrile within 72 hours and showed no relapses. All the patients recovered without any serious complications incident to the disease or to the penicillin treatment. E Hinde.

HYND R. S. The Construction of Army Huts to Limit Infestation by *Ornithodoros moubata* (Relapsing Fever Tick). *East African Med. J.* 1945 Oct., v 2, No 10 337-42, 2 figs.

To investigate the possibility of constructing a tick-proof hut a series of experiments were conducted with *Ornithodoros moubata* to discover the climbing powers of the tick the conditions necessary to make the tick leave the floor to climb and if projecting metal strips in walls would act as barriers to climbing ticks.

The experiments were carried out in a specially designed wooden box fitted inside with two projecting metal strips to act as obstructions to ticks attempting to climb up the sides. A glass observation panel was provided in one side. A second box to hold a guinea pig was fitted into the top of the first. The experiments are described and from the results the author concludes that, in lightly infested huts there is little urge for ticks to climb the walls they will do so in heavily infested huts and in those with impermeable floors in order to find cracks the climbing urge is not influenced by the presence of a living being metal strips (rough or smooth) set into the walls and projecting from them do act as barriers.

Therefore he makes the following suggestions earth floors should be avoided as they are the normal habitat of *Ornithodoros moubata* a hard floor free from cracks can be made of bitumen, concrete or beaten tar-and-earth it should be six inches thick and should have a metal strip inserted midway through its thickness and projecting three inches outwards all round. This will not, of course, prevent ticks being carried into the hut on the feet and clothing. A foot or so above the floor another metal strip should be inserted into the walls and this should protrude three inches all round the hut, both inside and outside. It is hoped that a test on a full scale model can be arranged, for if successful the decrease in the incidence of relapsing fever which could be expected if all huts were constructed in this manner might well be worth the additional expense involved in construction.

R S Lesson

## YAWS AND SYPHILIS.

DUVALIER, F. Contribution à l'étude du plan en Haïti. L'aspect médico-social et l'oeuvre de la Mission Sanitaire Américaine. [Contribution to the Study of Yaws in Haiti. The Medico-social Aspect and the Work of the American Sanitary Commission.] Reprinted from Bull. Assoc. Méd. de Langue Française de l'Amérique du Nord. L'Union Médicale du Canada. 1945 June v 74 20 pp 3 figs. 1 map & 1 chart. [37 refs.]

Ninety per cent. of the Haitians are illiterate and 80 per cent. of the rural population are infected with yaws. Hygienic conditions are very poor and nutrition is defective. The interrelationship of ill-health and low economic output is stressed. Yaws is particularly prevalent in the mountainous rural areas where difficulty of access is a hindrance to effective treatment. Cases secondary and tertiary were more numerous during the rainy seasons. The author thinks that yaws was endemic before Columbus landed, and also that it was spread through the Slave Traffic. During the American occupation

1915-1924 anti yaws work was carried out and rural dispensaries were opened, but from 1931 to 1942 this activity practically ceased. In 1943 a further campaign was started by the American Sanitary Mission but it was considered that treatment alone was not sufficient and that an approach should be made along the lines of social medicine. Anti yaws centres were opened. Mapharsen (3 intravenous injections of 0.6 [presumably a misprint for 0.06 gm.] at 8-day intervals) sulpharsphenamine and bismuth salicylate (3 intramuscular injections of 1.0 cc. [concentration not stated] at 8-day intervals) were used. The results with mapharsen were rather encouraging.

Although the social aspect is stressed the isolation and illiteracy of the population offer a tremendous barrier to any rapid achievement.

Any plan for the eradication of yaws in Haiti should comprise a rational organization of the rural area with construction of new roads and repair of existing ones the establishment of a normal standard of living for the natives and the education of the 90 per cent. illiterate population which seems hardly to have emerged from slavery.

C J Hackett

MONTEL R. Contribution à l'histo-pathologie de la lésion primaire d'inoculation et des lésions secondaires du pian. Chancres pianiques pianides pianomes [The Histopathology of the Primary and Secondary Lesions of Yaws.] *Bull Soc Path Exot* 1944 v 37 Nos. 3-4 71-84 8 figs on 4 pls & 1 text fig [23 refs.]

The author described in 1928 the primary lesion of yaws and contrasted it with the corresponding lesion of syphilis [see this *Bulletin* 1929 v 28 951]. He later pointed out that contrary to the general view secondary lesions were not merely disseminated primary lesions but distinct. In the present article he takes up this question again. He has studied minutely the microscopic anatomy and histology of 6 primary yaws chancres 2 secondary rashes and 5 pianomes (generalized lesions) and he describes the histology of twelve of these in great detail. The contribution is illustrated by excellent photomicrographs depicting the changes which he describes. Those interested should consult the original description which is very condensed and to convey the details to readers would entail almost a *verbatim* transcription. As described in the letterpress the histological differences are quite marked. Briefly the primary yaw is characterized by ulceration which destroys the upper layers of the skin and presents at the border a marked hyperacanthosis with depigmentation. One photograph shows this clearly. The epidermis is invaded by motile cells in tracks and small groups displaced by oedematous areas. Beneath this migratory cells densely infiltrate with a conglomeration of polymorphonuclear cells plasmocytes lymphocytes histiocytes and many eosinophiles and in the deeper parts of the dermis is a certain degree of sclerosis. Giant cells are never present.

In the second group of lesions the pianides the epidermis is thickened but there is no hyperacanthosis the migratory cells penetrate at isolated spots only. Infiltration is not marked and is situated mostly round the cutaneous vessels and hair follicles and is made up of lymphocytes and histiocytes rarely any polymorphonuclears. Plasmocytes are absent. In the pianoma which is a papilloma without ulceration the hyperacanthosis of the epidermis is great the crust is stuffed with migratory cells which have traversed the infiltrated epidermal layers. A thick plasmocytic barrage is present the vessels are congested, new capillaries formed, stuffed with eosinophiles and swollen endothelial cells. There are no giant cells and no sclerosis of the deeper dermal layers. The rest of the article is taken up in stressing with quotations from the literature the tendency on the part of those working on the pathology of yaws to confuse these changes and it ends with a brief statement of certain differences



which distinguish yaws lesions from those of syphilis namely that the yaws lesions tend to be dermatropic that the infiltration is largely limited to the sub-papillary layer vascular lesions are slight, infiltration is not nodular and perivascular and the deep vessels are not affected. There are others but these are the chief

H Harold Scott.

MONTEL, R. Les accidents secondaires cutanés du chancre roséole planides planomes [Secondary Rash in Yaws.] *Bull. Soc. Path. Exot.* 1944 v 37 Nos. 5/6 137-45 5 figs (4 on 2 pls.) [15 refs.]

In the author's view too little attention has been paid to some of the cutaneous manifestations of yaws and the inexperienced are apt to regard them as new conditions and to give them a variety of names. He describes secondary lesions of the skin under four groups (1) *Roséola* fleeting and therefore often unnoticed, and hence not mentioned by some and denied by others. It appears most commonly about 20 days after the primary sore. (2) *Planides* appearing in the interval between the roseola and the generalized eruption (which he calls planomas). They always precede the general eruption but may continue to coexist with it. He speaks of four kinds of planides (i) Furfuraceous circinate lichenoid or like pityriasis at one stage the condition resembles cutis asperna. The lesions are usually on the trunk, and cause considerable itching. (ii) Papular isolated or agminated papules in size from that of a lentil to that of a large pea buff or copper-coloured. They also cause itching, but usually regress spontaneously. (iii) Circular areas of desquamation erythematous and papulo-squamous on the palms and soles 1-2 cm. in diameter by fusion they may form curious geometric figures. (iv) Plantar hyperkeratosis often serpiginous and presenting a worm-eaten appearance. (3) *Mucosal lesions* on the lips and tongue in plaques resembling those of syphilitic leucoplakia, with well-defined border sometimes whitish or pearly or greyish yellow mammillated they may ulcerate. (4) *Pianomas* or vegetating papillomatous lesions oozing, but not desquamating. Of these also the author distinguishes four forms (i) Developing from the original yaw (ii) Resulting from transformation of one of his group 2 planides (iii) The generalized yaws eruption (iv) The confluent condylomatous yaws.

Although these are all detailed as distinct they do not always remain so and one may pass into another the papular planide (2 (ii) above) may become a papillomatous pianoma (4 (i) above) and the eruptive pianoma (4 (iii)) may become a vesicular papule or pustule (2 (ii)) but the author thinks it well to point out these various forms in order that their histopathology may be more closely studied. The article is well illustrated.

H Harold Scott

WHITEHILL, R. & AUSTRIAN, R. Further Observation on the Treatment of Yaws with Penicillin. *Bull. Johns Hopkins Hosp.* 1945 June v 78 No 6 274-94 10 figs

Forty-one Filian cases of primary and secondary yaws in which spirochaetes were found and the Kahn test was positive are reported. The infections had been present 1-12 months and severe moderate and mild cases were about equal in numbers. Only eight patients had received any previous specific treatment, the maximum being "five injections of arsenic" 9 months previously. Thirty of the patients were under fifteen years of age. Penicillin was given intramuscularly in doses of 15 000 to 30 000 units at intervals of 3-4 hours to total dosages of 100 000 to 2 400 000 units.

In all cases except three no spirochaetes were found 16 hours after treatment had started and in those three no spirochaetes were found after 24 hours. No Herxheimer reactions occurred. In 37 cases healing was complete in three weeks despite differences in total dosage. In the other four cases the healing of single lesions about the ankle caused the delay. (Perhaps some other cause was present in all these cases. The longest period of follow-up was 20 weeks (two cases) only 14 patients were observed for more than 10 weeks. In no case was a positive Kahn reaction permanently reversed, but no case receiving more than 1 200 000 units was observed for longer than 10 weeks. One clinical relapse after 230 000 units was observed nine weeks after admission.

The use of 100 000 units in four doses in 9-12 hours is probably as effective as many incomplete courses of arsenicals given over a longer period. It will cause the healing of secondary lesions and thus render the patient non-infectious at least for the time being. Further follow up work is being carried out at the Colonial War Memorial Hospital at Suva.

One case of tertiary yaws of five years duration in a child aged fifteen is reported. The skin and bone lesions responded more slowly but they had previously not healed despite prolonged and repeated arsenical and bismuth treatment.

GUTMARLES F N Penicilina pela boca Demonstraçao de sua atividade pela cura clinica da boubra (Nota prévia) [The Curative Action in Yaws of Penicillin taken by Mouth.] Hospital Rio de Janeiro 1945 Aug v 23 No 2 229-32 2 figs English summary C J Hackett

Demonstration of the activity of Penicillin by mouth was obtained by the clinical cure of three cases of yaws with primary and secondary lesions. The Wassermann reactions were negative in two cases after a month of observation but returned positive. The treatment consisted in 1 000 O u by mouth diluted in water each two hours (excepted at 24 and 2 o'clock) during 10 days. The total amount of Penicillin per patient was 100 000 Oxford units.

## LEPROSY

REVISTA BRASILEIRA DE LEPROLOGIA S Paulo 1945 Sept v 13 No. 3 133-227

The *Revista de Leprologia* in 1938 put forward the basis of a new clinical classification of cases of leprosy. In 1945 mainly at the instance of Dr Lauro de Sousa Lima doubts began to be expressed on the satisfactoriness of that classification and in view of the Pau American Congress of Leprologists which is to be held in Rio de Janeiro in 1946 the present is looked upon as a suitable time to reconsider the classification of cases of this disease.

This number of the *Revista* is devoted entirely to the subject. It opens with a reproduction of Dr Lauro de Sousa Lima's paper in which he stated that on certain points needing amplification or clarification in particular the difficulties in classifying the non-characteristic forms and those cases which undergo changes of type and intermediate relapsing cases. Examples are given where there is a conflict between the different factors of criteria in classification.

Thus (1) Cases clinically and histologically of the tuberculoid form but

BANCROFT H. GUIXTO R. S. RODRIGUEZ, J. V. & MARQUES A. P. A Note on Familial Relationship and the Risk of developing Leprosy *Internat. J. Leprosy* Cleveland, Ohio 1944 Dec. v 12 79-82.

In the Philippines the risk of infection of persons living in a house with a person suffering from lepromatous leprosy has been found to be eight times as great as that of those not known to have had such household exposure—these conclusions were formed on the basis of 283 families in Cebu Island P. I. with sufficiently complete records for analysis [this *Bulletin* 1936 v 33 931 1942 v 39 216 1944 v 41 48]. The duration of exposure to infection was expressed in person years—that is each year of life following exposure was counted as a year of risk. Only households in which the primary case was in a member of the family were included. The risk of infection from a neural case was no greater than for the general population. The highest rate of attack—4.31 per 1,000—was in a group exposed to an infected father—the rates in relation to mother, brother and sister varied between 3.57 and 3.60 only. The infection rates for males were always higher than for females except where the primary case was a mother—in that case the female rate was 8.10 per 1,000 against 1.95 for males—but that rate was based on too few cases (three females and two males) to be significant. Further inquiries on this important subject are needed.

L. Rogers

MOISER, B. Modes of Transmission of Hansen's Disease (Leprosy) *Leprosy Review* 1945 Dec. v 16 No 2, 63-6

The author states that leprosy is undoubtedly a house or family disease yet in S. Rhodesia 60.9 per cent. of over 2,000 cases failed to give a history of contact with another case. At his hospital cockroaches have been investigated with the help of a trained hospital orderly who carried out microscopical examinations and found acid fast oval bodies in 69 per cent. of those obtained in the hospital or from kraals some distance away. Similar bodies were not found in other insects examined. They were also found in the dried droppings of the insects in which they survived for 169 days. He says that cockroaches bite man savagely at night but those caught in native huts and not fed on leprosy material also were found positive to "Hansen's bacillus". It is not stated on what ground the acid-fast bacilli in the cockroaches were determined to be those of Hansen but the author concludes that these investigations give some reason to doubt an exclusive contagion and infection theory of the transmission of Hansen's disease from man to man.

In an editorial it is recorded that Professor Buxton was consulted on this paper and he pointed out that cockroaches eat a great variety of types of food, and may be expected to swallow many types of bacteria, some of which may belong to the large group of acid fast bacilli which are therefore probably normal inhabitants of these insects.

L. Rogers.

MONTIEL, R. BRUX Mlle. & MARIANGEAS Mlle. La bacillémie lepreuse techniques de laboratoire pour sa recherche [Bacillæmia in Leprosy Laboratory Techniques for its Study] *Bull. Soc. Path. Exot.* 1944 v 37 Nos. 9/10 261-4 3 figs.

In this note the author deals with the methods of demonstrating lepra bacilli in the blood. He points out that the organisms are found in the large monocytes which are more numerous in blood taken from the ear under pressure, than in that from a finger. They may more readily be demonstrated in blood taken from a vein if 5 cc. are centrifuged after being received in a little citrate solution.

and if a preparation from the leucocyte layer is stained. Numerous bacilli are found in the protoplasm of the large monocytes and those free in the circulation are derived from ruptured leucocytes. L. Rogers

MOSE A M & BASOMBRIO G The Diffusion Factor in Leprous Skin. *Internat J Leprosy* Cleveland Ohio 1944 Dec. v 12 49-59 4 figs. on 1 pl [18 refs]

The diffusion factor dealt with by the authors is measured by injecting into the shaved skin of a rabbit a 1 per cent solution of trypan blue as an indicator together with the tissue extract to be tested and measuring the rate of diffusion around the site of injection. Testicular extract has the highest rate of diffusion. Tests have been carried out to compare the diffusion factor present in normal and in leprosy skins and it has been found that tuberculoid skin has a diffusion action nearly equal to that of normal skin but that the activity of lepromatous skin is considerably less and is similar to that of a saline control. The factor in skins containing different numbers of lepra bacilli were also measured and it was found that the diffusion activity of lepromatous skin is inversely proportionate to the amount of *Mycobacterium leprae* it contains. Further an extract of lepromatous skin appears to be antagonistic to the diffusion action of an extract of tuberculoid skin. [See also this *Bulletin* 1944 v 41 582] L. Rogers

TILDEN I L. Lepromatous Leprosy a Reticulo-endothelial Disease. *Histopathologic Aspects*. *Am J Clin Path* 1945 May v 15 No 5 165-77 12 figs [14 refs]

This is a detailed and well illustrated account of the microscopical characters of lepromatous lesions. The author supports the view of ASCHOFF regarding the reticulo-endothelial system which is especially involved in lepromatous leprosy with abundant lepra bacilli in the affected tissues and negative lepromin tests. The nodules are predominantly composed of histiocytes mostly spindle-shaped resembling fibroblasts. The epidermis over a nodule becomes atrophied and the papillary portion is often obliterated. When the tissue is stained with Sudan III there is a striking resemblance to xanthoma with varying amounts of lipid material. Countless numbers of lepra bacilli are present, mostly arranged in parallel bundles. The globi are simply large or fused histiocytes forming giant cells. Another important feature is the absence of any necrosis such as is a typical feature of tuberculous lesions. The liver and spleen commonly show foci of similar involvement of reticulo-endothelial tissues with circumscribed milium lepromata most clearly seen in the liver. The lymph nodes are also affected with coarsely vacuolated cytoplasm. The glomerular tufts of the kidneys may show amyloid changes. The lungs are the least affected of the internal organs. Among 16 autopsies tuberculous complications of leprosy were found in 7 L. Rogers

DAVISON A R Notes on a Case of Lymphadenoma complicating Leprosy *Internat J Leprosy* Cleveland, Ohio 1944 Dec. v 12 33-40

The main interest in this case is that the development of symptoms of lymphadenoma in a lepromatous case in a European was followed by a remarkable change from repeatedly positive to repeatedly negative bacteriological examinations for lepra bacilli during the last two years of the patient's life. The treatment used at Pretoria was the usual one by subcutaneous and intradermal injection of chaulmoogra esters under which 20 to 30 per cent of the neural cases are discharged each year. In the case of lepromatous disease on the

with the organism of tuberculosis. To test this theory, the response of persons in non-endemic areas in the form of both early and late reactions has been tested. The results in ten patients with various dermatoses showed 9 early and 8 late positive reactions. Of four patients with Boeck's sarcoid three gave negative results and one was weakly positive. At Seaview Hospital, New York, 108 patients with pulmonary tuberculosis were tested: the early (Fernandez) reaction was positive in 43 (70.4 per cent.) of 61 tested and the late (Mitsuda) reaction was positive in 50 (46.2 per cent.) out of 108. *L. Rogers.*

FENNEL, E. A. Leprosy. Initial Lesion and Surgical Cure. A Case Report. *Internat. J. Leprosy*, Cleveland, Ohio 1944 Dec. v 12 83-9

This paper records the present condition of two surviving leprosy patients in whom the primary lesion was removed surgically many years ago: they were first reported in 1937 see this *Bulletin* 1938 v 35 300. The first patient had voluntarily lived and worked in the Hawaiian leper settlement. In September 1932 he developed a solitary pink macule on his forehead and a second one a little later: in one of these the typical lepra bacilli were found in 1933 which did not produce any signs of tuberculosis or leprosy on inoculation into guinea-pigs. Histologically tuberculoïd changes were found in the excised lesions. Repeated subsequent bacterioscopic examinations have all been negative for lepra bacilli and he has remained free from other symptoms of the disease up to the present time: eleven and a half years after the little operation.

The second case is in the female child of leper parents in Hawaii, both of whom had neural symptoms: but she was removed from them at the age of six hours and brought up in a clean nursery (see GOODRICH & MCCOY this *Bulletin* 1916 v 8 243). While she was still an infant, a reddish brown nodule 12 by 8 mm. in extent and 2 mm. high on the flexor surface of the left forearm had been excised and a moderate number of lepra bacilli were found in it microscopically. The histology was entirely consistent with a leprous nodule. Seven months after the operation a few atypical acid-fast bacilli were found in a stamp from the scar: so she was declared to be leprous and continued to live in the settlement presumably with her leper parents. At the age of ten a careful examination failed to reveal any signs of leprosy: at seventeen she married a heavily infected lepromatous leper with marked nodules. In 1937 she applied for and obtained parole and was found, after thorough microscopical examination, still to be free from all signs of the disease. In 1944 she was again examined clinically and showed no evidence of leprosy: so she has remained free in the disease for nearly thirty years. These cases afford a strong argument early diagnosis.

[It may also be pointed out that these cases strongly support the modern view that leprosy infection usually occurs through the entry of the causative bacilli into the skin through abrasions etc. including the punctures of insect bites: to form at first an isolated local infection.] *L. Rogers.*

MUIR, E. Preliminary Report on Diasone in the Treatment of Leprosy. *Internat. J. Leprosy*, Cleveland, Ohio 1944 Dec. v 12, 1-6.

In view of the favourable results of the use of the closely allied promin at the U.S.A. Carville settlement, and the favourable results reported from the administration of diasone in tuberculosis: the latter drug has been tried by the author in lepromatous cases in the Trinidad Charachacare Island leprosarium. Diasone was given intravenously in doses of 0.3 gm., the powder being dissolved or suspended in 1 cc. of sterile normal saline and the fluid filtered through three layers of sterile gauze. The injections were given six days a

week and the dose was gradually raised to 2-8 cc. In view of the anaemia producing action of the drug the dosage was controlled by watching the haemoglobin index. The early results—rapid clearing up of lepromatous ulcers and improvement in the general well being of the patients—inspired their confidence in the treatment but in some the appearance of anaemia and weakness led to the suspension of the treatment or a diminution of the dosage. Later the injections were restricted to three a week with dosage varying from 2 cc. to 8 cc. At first twelve cases were treated, but later the number was raised to about 100 in about half of whom the drug was given orally in capsules. If the haemoglobin fell below 78 per cent. ferrous sulphate was given orally. Beneficial results were noted in the form of general improvement in health, drying up of lepromatous ulcers and flattening of nodules, clearing of nasal lesions and of inflammatory eye lesions and disappearance of chronic fever and lepra reaction. Of 33 cases treated for over three months by intravenous injection 17 had greatly improved 15 were slightly improved and 1 remained stationary. Of 10 cases treated orally for over three months 7 had greatly and 2 slightly improved. In cases treated by either method for less than three months none showed great improvement but 36 out of 41 showed slight improvement. There was no evidence that changes in the haemoglobin content influenced the effects of treatment. Liver extract and iron in most cases improved any anaemia. The good effect in clearing up febrile and inflammatory symptoms was noteworthy. The results are therefore encouraging and are very similar to those produced by promin.

L. Rogers

CHORDNE V. Action thérapeutique du para amino-phényl sulfamide et de l'acétamide employés soit séparément soit associés dans la lèpre [The Therapeutic Action of Sulphanilamide and Acetamide separately and together, in Leprosy] *Bull Soc Path Exot* 1945 v 38 Nos 7/8 183-95

In this paper the author records experimental trials of acetamide and Septoplax [sulphanilamide] both separately and together with a control series in rat leprosy. Details of the experiment are recorded together with a table summarizing the results. Both local and generalized lesions were first produced by inoculating the rats with Stéfanaky's bacillus and leaving time for the general development of the infection. The acetamide was given orally in solution in large doses over a period of 117 days. In a second series of animals large doses of Septoplax were administered for a similar period. In a third series both were given but the combination proved to be toxic and the animals wasted. Both drugs caused reduction in the local lesions at the sites of infection and prevented the development of lesions in the internal organs but no better results were obtained by their simultaneous use than separately.

L. Rogers

LENGAUER L. Palm Oil in Leprosy *Leprosy Review* 1945 Dec v 16 No 2 67-9

Working in the Benin province of South Nigeria the author heard of a leper village which had been founded by an ex leper. This man was found to have extracted oil from the kernels obtained from available palm trees and to have used the oil extensively by rubbing it into his skin. He soon noticed improvement in his health. To increase his food at low cost he had also drunk the oil to the extent of half a teacup at a time. At the end of a year he had recovered, and he then began to treat other leprosy patients in the same way and soon a village had grown around his solitary hut. At the time of the visit

of the lady doctor the village was very clean and about 100 lepers looked well. They showed peculiarly smooth skins and tuberculous areas and macules seemed to be flattened, as if almost dissolved although no other treatment had been given. Only lepers from neighbouring villages were admitted. The author decided to try palm oil treatment herself and she found that chronic ulcers did very well under an ointment composed of zinc oxide powder mixed with palm oil. This oil, given orally in place of cod liver oil during the war was also beneficial, and relieved constipation. It is a cheap method of supplementing a deficient diet.

L. Rogers.

FAGET G. H. & FOGGE R. C. Penicillin used unsuccessfully in Treatment of Leprosy *Internat J Leprosy* Cleveland, Ohio, 1944 Dec. v 12, 7-10

This short note records the trial of penicillin in seven lepromatous or nodular cases of leprosy with negative results as regards the primary disease. Two of them showed recently developed nodules the third was a specially early case and the other four had more or less advanced lepromatous lesions. Complications included eye, nasal and laryngeal lesions. No beneficial effects were observed in these conditions with the exception of healing of secondarily infected ulcers in one case. The doses of penicillin used were up to 50 000 to 100 000 units daily for a period of several weeks. In an addendum written six months later the authors report that during that time no beneficial result attributable to the treatment had been observed in the seven cases first treated. Four others treated with much larger doses had also failed to respond to penicillin.

L. Rogers.

SLOAN N. R. Tracheotomy in Leprosy *Internat J Leprosy* Cleveland, Ohio, 1944 Dec. v 12 11-30 6 figs.

This paper deals with an extensive experience in advanced lepromatous cases at the Hawan Molokai settlement, where no less than 13.1 per cent. of "active patients" are wearing tracheal tubes. During a twelve-year period, 148 tracheotomy operations have been performed on 144 patients. Information is tabulated on the time from first isolation to operation and age at time of operation. Leprotic laryngitis is found only in lepromatous cases and it commences with great thickening of the epiglottis. Spread of the disease to the vocal cords produces stenosis requiring operative relief. Increasing hoarseness and dyspnoea, with choking spells are the main indications for the operation, which should not be delayed too long.

The surgical anatomy and operative procedure are fully described. After the operation a semi-sitting position for a day or two, codeine sulphate in half grain doses orally before meals for three days and liquid diet for a day or two are advised. Later the tube should be removed for cleansing twice a day. Relief is quickly afforded. Out of 89 cases tabulated, 14 deaths are classed as post-operative within two weeks and of the remaining 84 28 are classed as "tube deaths" in the sense that they were indirectly caused by the laryngeal lesion which necessitated the operation. The deaths from tuberculosis were only 15 to 18 per cent. about half the rate for the settlement at large. Those still living number 46 one of whom has worn a tube for six years.

L. Rogers

Dow D. Occupational Therapy in Leprosy Institutions. *Leprosy Review* 1945 Dec. v 16, No. 2, 57-63.

The author writes from experience at the Dichpali Leprosy Hospital, India, in which there are 800 resident patients, mostly men. He first stresses the

importance of studying the psychology of the patient as he holds that few if any of the patients are really healthy minded. The patient's sense of frustration should be removed and he should be helped to resume his place in society for which purpose he should be provided with suitable occupation and work of a useful nature to restore his self-confidence. Active outdoor agricultural work is best for those fitted for it but for others cooking and the preparation of grain etc. house cleaning the grinding of rice and flour are suitable occupations. It was not found possible to make weaving profitable. Women are employed in washing and mending clothes cooking light gardening etc. The older children do similar work to that of the women except for cooking. Each patient on admission is given a labour classification.

The original 50 acres of the colony have been increased to 450 acres of these 250 are devoted to agriculture with the help of irrigation from a tank and wells. The products are of financial importance but of more importance is the satisfaction and contentment of the patients as the result of doing interesting and productive work.

L. Rogers

LEPROSY REVIEW 1945 Dec. v 16 No 2 40-57 Preventoria. A Symposium on the Care of the Children of Leprous Parents.

The important subject of the best methods of protection from infection of children born to leper parents is summarized in an introduction by the Editor Dr E. MUIR. This was sent to several experienced workers for their comments which are recorded in this important article. The principles discussed are that children are specially susceptible to leprosy and should be separated from infective parents as soon as possible after birth. To effect this either the infected patient may be isolated or the child removed to the care of relatives or to a preventorium for such children usually under the care of missionaries as in India. It is easier to make such provision in a wealthy country like Brazil with its 22 preventoria than in poor countries. In Nigeria the position is difficult and the rearing of children apart from their parents is injurious to them for crèches in the tropics are very difficult to run efficiently.

In commenting on the above statement Dr MONEY of Nigeria thinks that closed cases are not dangerous even to infants at the breast. He agrees on the danger of rearing infants artificially in the tropics and in general with the principles under discussion. Where practicable the use of wet nurses is beneficial. Four years' experience of allowing closed cases to retain their children has justified itself.

Dr DAVEY also of Nigeria is in agreement with the principles. He tabulates information on 3 031 uninfected children of leper parents. The type of leprosy to which 1,935 children actually living with an infected parent were exposed was —active lepromata in 128 early lepromata in 261 simple neural leprosy in 576 tuberculoid leprosy in 977 in 43 the type was unstated. This constitutes a serious problem, for the cases dealt with form only about one-fifth of those of the province of Owerri and work on a large scale is necessary to prevent child infections by making suitable provision for the separate accommodation of children of parents with open leprosy. Weaned children should be sent to healthy relations and should be examined periodically. A small crèche is necessary to accommodate new-born children of lepromatous women in settlements.

Dr ROSS of Southern Nigeria, in a short note agrees with Dr Davey. Dr WHARTON in British Guiana has little difficulty as the sexes are separated at the Mahaica leprosy hospital and the few infants born are taken over by a relative or guardian usually within seven days of birth. Dr ROBERT COCHRANE in Madras recognizes the importance of the problem but in India, in the case of nearly all the children exposed to serious risk of infection relatives can usually



be found to take charge of the child, or the lepromatous parent can be isolated. There is still scope for healthy children's homes. Cochrane also advocates the separation of children from night contact with an open case in villages—there is evidence that this procedure produces good results.—

Lastly Dr John LOWE, of Calcutta, is in agreement with the above opinions, and as a result of his own experience emphasizes the danger of children remaining with leprosy parents even for 18 months from birth, for a number of them (25 of which are tabulated) developed signs of the disease later and had to be removed from healthy children's homes. He therefore advises the early adoption of infants by healthy relatives.

L. Rogers.

## HELMINTHIASIS.

SAUTET J & MARNEFFE H. Infestation naturelle de *Planorbis aduncus* Bourguignat 1879 par *Schistosoma mansoni* au Soudan Français. [Natural Infestation of *Planorbis aduncus* by *Schistosoma mansoni* in the French Soudan.] *Bull Soc Path. Exot.* 1944 \ 37 Nov. 9/10 320-21

In 1942, in the area of Bagueda, near Bamako French Soudan, where the villagers were heavily infested with rectal schistosomiasis snails of the species *Planorbis aduncus* were found naturally infested with fork-tailed cercariae. Mice were infested by placing them in water containing the cercariae and adult *S. mansoni* and their eggs were recovered from the mice especially from the liver

J F Corson

HERRÁNDEZ MORALES F. The Treatment of Schistosomiasis. *Puerto Rico J. Pub. Health & Trop. Med.* 1945 Mar r 20 No. 3 322-33. [Refs. in footnotes.] [Spanish version 339-56.]

After a "partial review of the literature" on the treatment of schistosomiasis with emetine and with antimony in its various forms there follows "an analysis of one hundred and fifty-seven cases of Schistosomiasis mansoni treated with Fouadin." The occurrence of this infection has become more prominent during the last few years in Porto Rico. Many persons are unaware that they harbour the infection and a large number of apparently healthy youths were rejected for military service on account of it. The disease now constitutes a public health problem of first importance to Porto Rico. Fouadin has been widely used in treatment with conflicting local views on its efficacy up to now there has been no proper analysis of the results of its employment. A cure rate of between 50 and 60 per cent. was obtained with Fouadin by the author after one or more courses of treatment of his cases. This is in accord with the experiences of others elsewhere. The criteria of cure were the disappearance of symptoms of eosinophilia and of ova from the stools. Ova usually vanished between the fourth and twenty-fifth days (usually by the thirteenth) (whether from the beginning or after the completion of the course of drug treatment is not clear). Toxic reactions caused by Fouadin were encountered, and in some cases were regarded by the author as severe.

A R. D. Adams.

LAVIER G & STEFANOPOULO G L'intradermo-réaction et la réaction de fixation du complément dans la distomatose humaine à *Fasciola hepatica* [The Intradermal Reaction and the Complement Fixation Reaction in Human Fascioliasis caused by *Fasciola hepatica*] *Bull Soc Path Exot* 1944 v 37 Nos. 9/10 302-8 [21 refs.]

The authors review many earlier papers in support of their view that contradictory statements occur in the literature about the value of the complement fixation reaction for the diagnosis of human fascioliasis. This review is useful because some of the papers summarized in it are not easily accessible or are not often quoted.

For their own work the authors prepared an antigen by Fairley's method, which was also used by STEFANOPOULO and PAYET (*Gaz méd de France* 1938 No 6 315) and for the preparation of filarial antigen by STEFANOPOULO and DANIAUD [this *Bulletin* 1941 v 38 156]. *Fasciola* obtained from the slaughter house were dried and powdered. One gramme of this powder was kept in 100 cc of physiological saline at 37°C. for one day and the supernatant fluid was filtered through a Seitz filter. For use it was diluted 1/4 or 1/5 or more. This antigen gave immediate intradermal reactions. After 3 to 5 minutes a weal with pseudopodia appeared which reached 3 cm in diameter erythema appearing later. One or two hours later both erythema and weal disappeared, but infiltration of the skin and tissues around the reacting area persisted for 4 to 6 hours. After 24 hours the reaction had disappeared entirely. Delayed reactions were not observed but some strongly positive subjects showed delayed phenomena such as generalized urticaria pain and swelling of neighbouring articulations. Two subjects showed nausea profuse diarrhoea lasting several hours lipothymie and signs of shock. Subjects sensitive to various proteins may give false positives but their reactions are usually surrounded by a smaller erythematous halo not more than 1 cm in width which disappears very quickly.

For the complement fixation reactions the authors used powdered *Fasciola* 1 gramme of which was kept in 100 cc. of absolute alcohol at 37°C for 24 hours filtered and then evaporated until when it was evaporated to one-third of its volume it usually became cloudy. Absolute alcohol was then added to the initial volume and the precipitate disappeared. This final solution formed the antigen. It was usually active at a dilution of 1/20.

The sera of five subjects affected with fascioliasis were used. The first had had fascioliasis for ten years the second had contracted it ten years before but was clinically cured and six months earlier the stools contained no eggs of *Fasciola* and there was no eosinophilia the third had had fascioliasis for ten years this subject was described by DALLAINES LAVIER and GANDBILLE [this *Bulletin* 1943 v 40 472] the fourth had had fascioliasis for 3 years but only a few eggs of *Fasciola* were present in the stools the fifth had had fascioliasis for 4 months and the positive intradermal reaction obtained was contemporary with the appearance of eggs of *Fasciola* in the stools. The controls were (1) the sera of 3 subjects infested with *Loa loa* the infestation of one had lasted 6 years that of another 7 years and that of the third 4 years (2) the serum of one subject harbouring *Taenia saginata* this subject had been treated for this condition the day before the tests were done (3) the serum of one subject harbouring *Echinococcus* cysts (4) two subjects serologically proved to be suffering from syphilis (5) the sera of 3 subjects without evidence of fascioliasis no eggs of *Fasciola* were found in the stools of these three subjects after repeated examinations but one had an eosinophilia of 50 per cent another a moderate eosinophilia and the third the normal number

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of eosinophils. Tests done with a filarial antigen and *Echinococcus* fluid showed that the controls with these infestations were positive to these antigens. A table gives the results. It shows that the *Fasciola* antigen was specific. All five subjects tested gave positive intradermal and complement fixation reactions to the *Fasciola* antigen and all were negative to the filarial and *Echinococcus* antigens except the subjects infested with these helminths. None of the controls reacted to the *Fasciola* antigen. The authors remark on the fact that the two syphilitics were negative to it although it has long been known that syphilis may give a positive complement fixation reaction to helminth antigens. They quote several papers which record this fact but point out that FAIRLEY showed that a suitable dilution of the antigen avoids false positives due to syphilis. The authors could not obtain a balharzial antigen but suggest that this antigen might give positive results with sera of subjects of fascioliasis because *Fasciola* and *Schistosoma* are nearly related. They suggest that the discordant results obtained by earlier workers may have been due to variations in the method of preparation of the antigen and to the fact that most of the reactions to which the authors refer were done upon sheep which often lose their infestations but retain antibodies when no flukes can be found in them. One of the human subjects tested by the authors had very strongly positive intradermal and complement fixation reactions although he had been for some months clinically cured. The implication presumably is that this subject had retained antibodies in his blood during this period.

MARTIN R. LE ROY STREAU B. RADOUOT P & BOURCART N. Un nouveau cas de distomatose hépatique diagnostic précoce par le tubeage duodénal. (A New Case of Hepatic Fascioliasis early Diagnosis by Duodenal Intubation.) Bull Soc Path Exot 1944 v 37 Nos. 11, 12 359-63 2 figs. [15 refs.]

The authors say that cases of hepatic fascioliasis have increased in numbers during recent years in France. They mention epidemics at Clermont Ferrand and Lyons. They think that, when a febrile syndrome with marked eosinophilia is encountered, every effort should be made to exclude fascioliasis. Early diagnosis is important because treatment with emetine is especially effective when the flukes are young.

The authors describe the case of a girl, aged 14 who was admitted to hospital with persistent fever lasting a month and a half. The history showed that three months before admission while the girl was on holiday in the country she complained of continuous headache pain in the right hypochondrium and at times belching vomiting. On her return to Paris the pain and vomiting had ceased but the girl was thin and had no appetite. Tuberculosis and typhoid infection were eliminated. The liver was painful and enlarged. Painful crises occurred which resembled hepatic colic. The spleen was palpable and there was slight xeroderma. Other examinations were negative except that the blood showed an eosinophilia of 46 per cent. Hodgkin's disease was eliminated by sternal puncture and the Casson and Weinberg reactions for hydatid disease were negative. Duodenal intubation then revealed the presence of eggs of *Fasciola* and examination of the stools subsequently also revealed them. The patient said she had never eaten water-cress (oregon) but she was very fond of eating herbs picked casually during her walks. [The doses given are not stated.] The number of eggs in the stools became smaller and smaller until none was found. The eosinophilia decreased to 20 per cent. but duodenal intubation still revealed eggs of *Fasciola* in the duodenum. A month later two duodenal intubations failed to reveal eggs. The authors remark that the painful enlargement of the

liver which is one of the cardinal symptoms of fascioliasis was absent from this subject the hepatic symptoms were only transitory. The patient however did show a symptom rarely recorded in subjects of fascioliasis namely enlargement of the cervical lymphatic glands. The palpable spleen is emphasized by the authors but this is an exceptional sign. They remark that the coexistence of an irregular temperature with profuse sweats and a high eosinophilia suggests fascioliasis. Duodenal intubation enabled them to diagnose the disease in this subject during the acute hepatic phase during which young flukes enter the liver before eggs of *Fasciola* appear in the stools. After this stage the subject often gets better and the infestation becomes chronic. In literature supplied to the authors by Professor LAVIER only 6 out of 127 cases were diagnosed during the acute early phase. Duodenal intubation can establish the diagnosis 15 days before eggs of *Fasciola* appear in the stools, so that emetine, which kills the young flukes more effectively than the older ones can be given.

G Lapage

ZAFHAROV V I [To the Epidemiology of the Alveolar Echinococcosis in Kazakhstan.]  
*Med. Parazit. & Parasitic Dis.* Moscow 1945 v 14 No 4 33-4 [In Russian.]

SCOTT J A. Hookworm Disease in Texas. *Texas Reports on Biol. & Med.*  
 1945 v 3 No 4 558-68 1 fig [14 refs.]

The available data indicate that in most of the parts of Texas where hookworm was once common the infection now occurs only in a very small percentage of the population and clinical cases are a rarity. In a small area in the extreme eastern part of the state the infection is more common but even there it is not more than half as frequent as it once was. A rough estimate based on the meager information available indicates that probably not more than 10 000 persons are infected and the number of clinical cases probably does not exceed 1 000. The improvement over conditions known to exist 30 years ago has probably been due in part to the control programs of various sorts. On the other hand in spite of depression set backs there has been a general lifting of the economic level of living in these areas which has undoubtedly been reflected in the decrease of hookworm prevalence through improved nutritional and sanitary conditions. There is a great need for further investigations to determine the exact public health status of hookworm disease at the present time and to define the conditions which might be modified so as to effect further control.

FISCHER F K. Beitrag zur Kenntnis der Anguilluliasis oder Strongyloidosis.  
 [Contribution to our Knowledge of Anguilluliasis or Strongyloidosis.]  
*Schweiz. med. Woch.* 1946 Feb 16 v 76 No 7 137-40 1 fig & 1 chart.  
 [21 refs.]

The author states that the records of strongyloidosis particularly reports on it in the German Ruhr district show that it often co-exists with hookworm infestation. He briefly outlines the life-history of *Strongyloides stercoralis* and reminds us that auto-infection can maintain an infestation the skin-penetrating larvae being able to develop either in the large intestine or in faecal matter adhering to the anal region and to penetrate either the mucosa of the large bowel or the perianal skin. The author states that few clinical papers report strongyloidosis as a serious disease, although ASKANAZY (*Cent. f. Bakt.*, 1 Abt. Orig. 1900 v 27 569) found in sections of the upper part of the duodenum and in the ileum severe damage done by the larvae which burrow into the mucosa of these parts of the intestine. The severity of any helminth infestation is however affected by the numbers of helminths present.

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The author reports in great detail his study of one patient infested with *S. stercoralis*. This patient was an Australian infantryman born in 1919 who had served in Palestine and Greece and had been captured in Crete in 1941. An epidemic of diarrhoea broke out in the unhygienic prisoners camp in Crete and the patient was severely ill in hospital. Transferred to Salonika and later to Athens, he suffered repeated attacks of severe diarrhoea and abdominal pain with flatulence. Treatment [unspecified] was given for dysentery "and living in Athens for a time he was recaptured and sent in 1942, to Italy where he was fairly well until in June 1942 he had another attack of diarrhoea, abdominal pain and flatulence lasting five weeks. He was again fairly well until June 1943 when the same symptoms recurred. In that year he reached Switzerland where in October 1943 he developed a sore throat and a rash resembling sudamina. Suspected of having measles he was sent to hospital where he had an attack of diarrhoea with blood and mucus in the stools and abdominal cramp. Examination revealed little likely to account for his illnesses. On October 20 1943 a differential leucocyte count showed that there were 53 per cent. of eosinophils in his blood. Agglutination tests ruled out typhoid, paratyphoid bacillary dysentery and brucellosis. The bloody diarrhoea continued, but the rash disappeared. On October 25 there were 16 per cent. of eosinophils in his blood. Neither *Entamoeba histolytica* nor its cysts were found in the stools, but these did contain larvae of *S. stercoralis* and eggs of *Ascaris* and *Trichuris*. On November 1 the subject was much the same and "Chenosis" expelled 5 *Ascaris*. There were then 32 per cent. of eosinophils in the blood. On November 6 there were 40 000 white blood cells of which 72 per cent. were eosinophils. Bone marrow obtained by sternal puncture revealed a very greatly increased formation of eosinophils. [Details of the differential counts of blood and bone marrow cells are given.] On subsequent dates the eosinophilia was as follows: Nov 8 77 per cent. (i.e. 3 000 of 40 000 white blood cells) filariform larvae of *Strongyloides stercoralis* were then numerous in the contents of the stomach and in bile obtained by duodenal sound. The bile also contained eggs of *S. stercoralis*. Nov 9 78 per cent. Nov 12 81 per cent. (i.e. 18 000 of 23 400 white blood cells). From this date this very high eosinophilia gradually decreased and with its decrease the patient felt much better and the diarrhoea ceased. On December 24 however the subject had marked pain in the penis and perineum with small haemorrhages from the urethra and swelling of the corpora cavernosa extending back to the perineum. There were very painful erections and reddening of the skin on the under side of the penis. The white blood cells rose from 9 800 to 16 000 with 41 per cent. of eosinophils. This condition disappeared in three days. By January 12, 1944 no larvae of *S. stercoralis* were found in the duodenal contents. The patient left for Australia with an eosinophilia of 35 to 45 per cent. A subsequent message from Australia said that he had felt well until February 1945 but still had larvae of *S. stercoralis* in his stools.

Discussing this case the author points out that *Strongyloides* can be distinguished from hookworm by the fact that its eggs are never found in the stools they can only be obtained either by a very drastic purge or by duodenal intubation, and then are seen to be always embryonated while the eggs of hookworms are not. The author never found the filariform larvae of *S. stercoralis* may cause sensitivity of the skin so that itching and the formation of weals may occur in the perianal region. A condition resembling "creeping eruption" may be established, and FULLEBORN (*Ann. Wack.*, 1925 v 35 1709) described the formation of similar weals on the skin of subjects infested

with *S. stercoralis* after injection into the skin of an antigen made from dried and powdered *Strongyloides* larvae. The urethral haemorrhages and the pain and itching of the penis of this patient are ascribed by the author to this cause. When the patient washed these parts with soap and applied 10 per cent. *Ung. Hydrarg. praec. alb.* these symptoms did not reappear [cf. the infestation of the genito-urinary tract with *S. stercoralis* described by WHITEHILL and MILLER, this *Bulletin* 1945 v 42 576].

Enormous eosinophilia such as that here recorded is unusual. It has been ascribed to an allergic condition in subjects with an eosinophil constitution, but Fischer suggests that in this patient a toxic effect was responsible. The patient was treated for 9 months but both adult *Strongyloides* and its larvae remained. He was however in good health, when he had an eosinophilia of 30 per cent. and larvae were not so numerous in his stools after treatment.

Gentian violet in doses of  $6 \times 0.04$  g. daily for about 3 months produced no improvement; larvae remained in the stools. Gentian violet was therefore combined with the following additional treatment which was given at the same time. The patient was prepared with a saline purge. In the forenoon he had an enema of 1 per thousand thymol solution or benzene water and on the following morning oil of chenopodium (two doses of 18 drops with 1 hour's interval between) followed at intervals of one hour by three doses of one tea-spoonful of sulphur depuratum. In the resulting diarrhoea massive numbers of dead *Strongyloides* larvae were found. This treatment was given 3 times at intervals of 8 days at the same time as the gentian violet and it produced no untoward results. No better results were obtained with filix mas, santonin or thymol. Carbon tetrachloride, tetrachlorethylene, atabrin, intravenous neosalvarsan, intravenous arsacetin, kamala, areca seed and Fouadin were all ineffective. Phenothiazine was also ineffective and had to be given up on the seventh day because it caused the excretion of porphyrin. A final attempt to cure the subject by duodenal intubation of 1 per cent. aqueous solution of gentian violet caused nausea, vomiting and collapse and the subject's departure to Australia prevented further trials of it. The author says that he gave in this way 250 cc. of the 1 per cent. solution of gentian violet at the rate of 50-60 drops a minute. [CRAIG and FAUST *Clinical Parasitology* 3rd edition 1943 253 recommend 25 cc. See also v ENGEL, this *Bulletin* 1945 v 42 49 who also began with 250 cc. but because of its severe effects substituted 100 cc. at a slower rate and claimed to have cured his subject. See also the other references mentioned in this abstract and PALMER this *Bulletin* 1945 v 42 135.]

G. Lapage

DROUET P. L. THOMAS C. HERBEUVAL R. & FAIVRE G. Hémorragies du vitré et ascariidose. Nouvelles hémorragies du vitré et néphrite consécutive à une intradermo-réaction à la toxine ascaridienne. [Haemorrhages of the Vitreous and Ascariasis. Fresh Haemorrhages of the Vitreous, and Nephritis, following an Intradermal Reaction to the Ascarid Toxin.] *Bull. et Mém. Soc. Méd. Hôp. de Paris* 1945 Nos. 24/25 342-4.

The authors describe the occurrence of bilateral haemorrhages into the vitreous humour of the eye of a woman aged 60. Clinical examination revealed nothing likely to account for these but the blood contained 22 per cent. of eosinophil leucocytes and about a year later when the haemorrhages recurred 18 per cent. of eosinophils. The stools contained eggs of *Ascaris* and *Trichuris*. Santonin at first failed to expel any nematodes (perhaps because the doses were too small) but later it expelled some ascarids. The eosinophilia persisted. The authors discuss possible causes of the haemorrhages but come to

the conclusion that they were associated with the ascariasis. Haemorrhages in the course of ascariasis have been noted by CASSOUTE and VAGUE (Soc. Péd. 1934 Jan. 16) MATHIEU and FAIVRE (Soc. Méd. de Nancy 1945) reported repeated haematuria coinciding with the expulsion of an *Ascaris* through the mouth but haemorrhages of the vitreous have been still more rarely reported in subjects infested with various parasites. In this subject however the eosinophilia persisted. The complement deviation reaction failed to reveal the presence of antibody in the blood, but this was not surprising because this antibody appears the authors state only when the cuticle of the nematode is ruptured or its permeability is altered by its death (cf hydatid cysts). The authors did intradermal reactions on this subject with the dilute coelomic fluid of *ascaris* derived from the subject under consideration. With a dilution of 1/100 of this fluid they obtained on two separate occasions a non-pruriginous papule the size of a 50 centime piece which appeared in a few minutes and disappeared after 1 hour. The same test gave the same result two days later. Two days later still a test was done with "*Ascaris* toxin" (the precise method of preparation of this is not stated). Almost immediately this "toxin" produced a non-pruriginous cockade reaction 2½ cm. in diameter with a haemorrhagic centre and erythematous periphery sprinkled with petechiae and an intermediate zone. A control intradermal reaction on a subject also infested with *Ascaris* but without any signs of similar haemorrhages into the vitreous produced in half an hour a non-pruriginous erythematous weal which disappeared in three-quarters of an hour. In several subjects not infested with *Ascaris* neither early nor delayed reactions were obtained.

About 4 hours after the intradermal reaction the subject under discussion showed a renewed haemorrhage in the temporal region of the right eye. She complained of lumbar pain. Next morning there was palpebral and malleolar oedema. The urine contained albumin, granular and hyaline casts, renal cells, red blood cells and polymorphonuclears. There were no other clinical symptoms. Two days later the oedema had disappeared, the urine contained a few erythrocytes and less albumin and urea but no casts. There was a blood eosinophilia of 10 per cent. Some days later the subject went home without any trace of nephritis.

The authors thus obtained experimental proof that "*ascaris* toxin" was the cause of the haemorrhages into the vitreous of this subject, but the nephritis and haematuria were new factors. The authors ascribe it not to an anaphylactic reaction, but to what TAYLOR has called renal intolerance. It resembles allergic nephritis. The intradermal reaction done with "*Ascaris* toxin" precipitated in this previously sensitized subject a true phenomenon namely a local haemorrhagic crisis which became general and attacked the eye and the kidney in which there was a temporary allergic haemorrhagic nephritis. We know that certain organs and especially the kidney are apt to show haemorrhagic reactions. Perhaps there was some individual cause in this subject to explain the localization of the haemorrhages in the eye.

Among authors who have studied the intradermal reaction to *Ascaris* "toxin" are CIRCULESCU (Soc. Méd. des Hôpitaux de Bucarest 1927 April) AVRAMOVIĆ and DANCILLA (Rev. Péd. et Pédicuit. 1937 December) and SIMONIN (Thèse Nancy 1919).

G. Lapage

THOMPSON E. J., RUFKIN H. & ZARROW M. Early Filariasis in Young Soldiers. Clinical and Pathologic Analysis. *J. Amer. Med. Ass.* 1945 Dec. 13 v. 129 No. 16 1074-9 [13 refs.]

A series of 200 young American soldiers infected with filariasis [presumably Bancroftian] has been studied during a period of two years. As a result of

prolonged clinical observation with biopsies of superficial lymphatics or lymph glands and the employment of a skin test using for this a *Dirofilaria immitis* antigen in various dilutions a concept of the pathology of early filariasis has been elaborated. The early stages of the disease are very different from the later classical elephantoid stage described in textbooks. After describing the six clinical groups into which their cases fall the authors conclude that there is no one symptom or sign that is constantly found in all cases of the early disease other than persistently enlarged and palpable lymph nodes. These in the earliest acute phase are large and soft but later they shrink and become hard. The differential diagnosis of the gland enlargement of early filariasis is dependent on biopsy of lymph cords and lymph glands and on the employment of the skin test described in detail by the authors. The biopsies were performed on superficial lymphatics and glands and where funiculitis was present material was taken from the pampiniform plexus under local anaesthesia. In the examination of lymph glands the authors found that the axillary glands were more likely to give a distinctive microscopic finding than the inguinal glands and they warn against the obvious temptation to take the latter purely on account of easier accessibility. They regard the lymphatic involvement during the first phase of the early stage of the disease as systemic rather than focal in origin and prefer to examine a lymphatic cord or gland bizarrely situated as long as it shows evidence of acute involvement. There is little to be learned from the incidence of primary lymph gland involvement. As a result of their studies they conclude that early filariasis can be divided into three phases—(a) the early acute or allergic (b) the subacute (c) the early chronic as follows—

(a) The *early acute phase* is characterized clinically by sudden lymphangitis with an accompanying lymphadenitis of the regional lymph glands lasting for 3-4 days. Fever and constitutional upset are minimal. Though the lymphangitis extends as a rule in the normal direction in some cases it is retrograde or centrifugal in its extension. The attacks may recur over 8-9 months or they may be single events. At the height of the lymphangitis in the arm leg or structures of the cord there may be lymphadenitis and lymphangitis bizarrely situated elsewhere. Funiculitis and epididymitis were seen in about half the cases usually these are unilateral although succeeding attacks may involve the opposite side they may subside rapidly with the declension of the lymphangitis. In association with them the inguinal glands are slightly enlarged and there is commonly an associated small hydrocele and a brawny oedematous thickening of the scrotum. The cord may become as thick as the thumb and the vas deferens as thick as a lead pencil.

During this stage no microfilariae are to be found in the blood even when a concentration technique (Knott's) is used. Eosinophilia is slight or moderate. Biopsy shows hyperplasia of the lymph follicles with eosinophilic infiltration and general oedema of the lymph glands. In many cases filarial worms are actually to be seen in the gland but the pathological picture apparently is not dependent on the visible presence of the worms. Lymph glands show similar pathological changes—thus supporting the view that the changes are of a generalized systemic nature and not purely focal.

Biopsy of an acute filarial lymph channel shows thickening oedema and eosinophilic infiltration of the wall. The lumen is filled with an acute thrombus in which the eosinophils are pyknotic and aggregated into a necrotic amorphous mass. Filarial worms or microfilariae may or may not be seen in the lymphatic vessel.

(b) In the *subacute phase* there is no lymphangitis swelling or oedema but a feeling of heaviness and aching of the involved part is experienced with little



cent. (38 out of 40) subjects without microfilariae were positive to a dilution of 1:10,000 of the *D. immitis* antigen. The percentage of positives and negatives to the other dilutions of the various antigens was of the same order.

With regard to cross reactions with other nematodes the authors found that among the 180 subjects in group A 127 (70 per cent.) had either *Ascaris Trichuris* or "hookworm" *i.e.* 63 (75 per cent.) of the 90 with microfilariae in their blood and 59 (66 per cent.) of the 90 without microfilariae. None of group B however had intestinal nematodes. All the subjects in group B were negative to dilutions of 1:200 and 1:10,000 of the three filarial antigens except two subjects (12 per cent.) who gave positive reactions to *Ascaris* antigen and also to physiological saline. The authors think it unlikely that these two positive subjects were suffering from early or low-grade infestations. They point out that CULBERTSON, ROSE and DEMAREST (*loc. cit.*) and BOZICEVICH and HUTTEN [this *Bulletin* 1944 v 41 1055] also obtained negative reactions to 1:200 and 1:8,000 dilutions of rat and dog filarid antigens in Americans not infested with nematodes.

These results suggest that skin reactions to filarid antigens may be greatly influenced by the presence of other nematodes. The presence of group-specific substances is also suggested by the fact that 83 per cent. (17 out of 24) of subjects in group A without microfilariae in their blood gave positive reactions to 1:10,000 dilutions of *Ascaris* antigen and 75 per cent. (15 out of 20) of subjects with microfilariae gave positive reactions to 1:10,000 dilutions of hookworm antigen. Similar results were obtained in those members of group A who had no microfilariae in their blood. The authors think that subjects with any of the nematodes may become skin sensitive to antigens from any member of the group. They refer to BACHMAN and RODRIGUEZ MOLINA [this *Bulletin* 1933 v 30 222] who reported positive skin reactions to hookworm antigen by subjects without hookworm infestation but with infestations with *Ascaris* and *Trichuris* to RODHAM and DUBOIS (*ibid* 1932, v 29 83) and BRUNNER (*J Immunology* 1933 v 15 83) who found that *Ascaris* antigens give positive reactions when other species of nematodes are present and to MAZZOTTI and OSORIO [this *Bulletin* 1944 v 41 857] who obtained 13 per cent. of positive reactions to *Onchocerca caenotensis* antigen by subjects not infested with this species.

The percentage of positive reactions obtained by the authors to the 1:10,000 dilution of *Dirofilaria immitis* antigen in the Porto Ricans of Group A, namely 87 per cent. far exceeds the estimated percentage infestation of the general population of Porto Rico namely 9.7 per cent. recorded by HOFFMAN, MARIN and BURKE [this *Bulletin* 1932, v 29 768].

The skin test for filariasis can thus only be used with safety when other species of nematodes are absent. This is a serious limitation of the test, because members of the Forces and others will be exposed to both filarids and intestinal species.

G. LaPage.

MAZZOTTI L. & OSORIO Maria T. The Diagnosis of Enterobiasis. Comparative Study of the Graham and Hall Techniques in the Diagnosis of Enterobiasis. *J Lab & Clin. Med.* 1945 Dec. v 30 No. 12 1046-8.

“Examinations for the diagnosis of enterobiasis were carried out in 430 individuals using both the Hall and Graham techniques. The percentage of positive results obtained was 32 per cent. with the Graham method and 16 per cent. with the technique of Hall.”

## DEFICIENCY DISEASES

CHURCHILL, M H Dietary Deficiency Diseases among Prisoners of War *J Roy Army Med Corps* 1945 Dec. v 85 No 6 294-8

This paper is based on notes of nearly 500 cases of deficiency disease occurring in prisoners of war in Singapore and Thailand during the period 1942-1945. Elaborate examination was often not possible and treatment was difficult owing to lack of supplies.

A type of amblyopia was a common condition—the first cases appeared within 4 months of the prisoners going on to the Japanese ration scale. In rather less than half the sufferers there was an association with some better recognized symptom of deficiency. The outstanding symptom was blurring of vision but this was preceded by smarting of the eyes, lachrymation and photophobia. The failure of sight was often progressive and severe; in other cases it progressed to a certain stage and then remained stationary; in others again it varied, improving when there was any substantial improvement in the diet. Two factors seemed to be concerned in producing the condition: dietary deficiency and intense sunlight. There was no apparent correlation between the defect in vision and the ophthalmoscopic appearances. About half those examined showed some degree of cupping or excavation of the disk.

Observations on pellagrous conditions, on beriberi and on some other aspects of vitamin deficiency are recorded. No evidence was found of deficiency of vitamins A and C.

H E Harding

KRISHNAN B G RAMACHANDRAM S & SADHU K. The Treatment and Prevention of Vitamin-B<sub>1</sub> Deficiency in Infants—a Public Health Experiment. *Indian Med Gaz* 1945 Oct. v 80 No 10 521-4

Infantile beriberi is far from uncommon in the Northern Circars of Madras Presidency and an inquiry centre was set up in Cocanada in 1942. This paper gives an account of its activities. The authors start by describing the disease which is vitamin B<sub>1</sub> (or thiamin) deficiency in infants of beriberi mothers and which differs in most respects from beriberi in adults. The symptoms may set in abruptly in an infant apparently in good health with cyanosis, dyspnoea and tachycardia and may run a fulminating course ending fatally in a few hours. In others there is colic with fits of screaming, vomiting, diarrhoea and convulsions. Still more chronic cases occur which are characterized by pallor, vomiting and signs of marasmus. Aphonia is a common symptom. Injection of vitamin B<sub>1</sub> brings about dramatic cures even in infants seemingly moribund.

At the Cocanada centre 1 145 infants had been treated by the end of 1945 all were breast fed and their ages ranged up to 12 months but most of the cases were in those under 6 months and the peak was at about 4 months. Of the total 980 (85.5 per cent.) were discharged as cured, but in 68 (6.9 per cent.) of these relapse or recurrence took place at intervals up to 3 months. Only 16 deaths occurred. Prophylaxis—giving one tablet of the vitamin (1 mgm.) to the mother once each day during 3 months before and 6 months after delivery—was tried and of 54 so treated, who had previously lost babies 28 had infants which developed the disease in spite of the vitamin administration. Twelve others with a similar history but who were not given prophylactic vitamin tablets had 8 living children all of whom developed infantile beriberi and were cured. The dosage used 1 mgm. tablets administered regularly seemed to be of some value, but was probably inadequate for the women were living on a diet very deficient in vitamin B<sub>1</sub>.

and hookworms was however not constant one third of the recruits with under 11 gm Hb had no infestation while one-third of those with moderately heavy infestations had over 14 gm Hb. It was concluded, therefore that hookworm infestation was a secondary factor in the production of the anaemia.

Over three-quarters of the total anaemia in all classes was normocytic (MCV between 80 and 100  $\mu$ ) In both Madras and Punjab about 60 per cent. of the normocytic anaemia was normochromic (MCHC 30 per cent. or over) but in United Provinces recruits 90 per cent. was normochromic and only 10 per cent. hypochromic (MCHC less than 30 per cent.)

In both Madras and Punjab about 20 per cent. of the total anaemia was microcytic (MCV less than 80  $\mu$ ) and about half the microcytic anaemias were normochromic. In United Provinces recruits only 2 of 39 cases of anaemia were microcytic and both these were normochromic.

Only five very mild cases of macrocytic anaemia (MCV of 100  $\mu$ . or over) were found. Two were from Madras two from United Provinces and one was from Sind. One of the Madras had a hypochromic macrocytic anaemia, and the remaining four were normochromic none had bilirubinaemia or splenomegaly. No case of macrocytic anaemia was found in the Punjab.

In both Madras and Punjab about 45 per cent. of the anaemia was hypochromic, but in United Provinces recruits the proportion was only 10 per cent. The frequency of hypochromic anaemia was greater among the severe anaemias where the haemoglobin value was below 10 gm. 11 out of 13 cases were hypochromic. Extreme hypochromia (MCHC less than 28 per cent.) was rarely seen except in the more severe anaemias only three of fifteen such cases having over 11 gm Hb. Contrary to expectation hypochromia, a sign of iron deficiency was not more frequent in men infested with hookworms than in the non-infested.

Whereas 56 per cent. of recruits with haemoglobin levels over 14 gm. had a MCHC of 32 per cent. or over this value was exceeded in only 35 per cent. of the normochromic anaemias. This difference is statistically highly significant but while red cells with a MCHC below 30 per cent. are certainly unsaturated, those with a MCHC a little over 30 per cent. may be saturated or unsaturated.

The change to army life and diet in itself, considerably improved the anaemias of the recruits but a group given in addition 8 grains of ferrous sulphate daily improved very much more. On recruitment, both the group given iron and the untreated group contained about 45 per cent. of anaemic men and about 25 per cent. of men with haemoglobin levels of 14 gm. or over. After 3 months training 31 per cent. of those not receiving iron were still anaemic and 50 per cent. had 14 or more gm. Hb. whereas of those taking iron only 8 per cent. were anaemic and 80 per cent. had levels of 14 gm. or more. Two months later those taking iron had improved still further but no significant change had occurred in the others. The observations showed that in both groups men with initial haemoglobin levels of between 14 and 14.9 gm. were capable of improvement. All types of anaemia seemed to respond equally well. Hookworm infestation had no measurable influence on the haemoglobin regeneration in either group even when the infestation was moderately heavy. The responses of the Madras and Punjab were very similar but in both groups the haemoglobin classes of United Provinces recruits were slightly inferior. The red cell count and packed cell volume both rose with the haemoglobin and were significantly higher from one month onwards in those taking iron than in those not taking it.

There were many puzzling features about this universal response to iron therapy. Only 4 per cent. of the men who benefited from iron had typical iron-deficiency anaemias and only 30 per cent. had any of the usual signs of iron deficiency. Furthermore, nutrition workers have deduced from analyses

that even the poorest Indian diets have an iron content adequate even for the greater needs of women. It is possible that a great part of the iron of the poor Indian diet is for some reason not assimilable. Apart from the original chemical form of the iron there is little knowledge of the influence on its absorption of mineral balance and such interfering substances as phytic acid. It is also possible that some dietary deficiency that may be the major cause of the anaemia prevents the utilization of iron and that when that factor is replaced iron is still necessary to build new haemoglobin. Finally it is possible that the benefit observed was due not to iron but to traces of some other metal present in the ferrous sulphate and deficient in the common Indian diet. Beyond speculation however it is clear that most recruits benefited from a daily dose of ferrous sulphate. The authors suggest that only when the haemoglobin level exceeds 15 gm should it be considered satisfactory—a standard reached by only 25 per cent of the newly joined recruits other than nursing sepoy.

F Murgatroyd

MOORE C V, BIERBAUM Olga S, WELCH A. D & WRIGHT L. D. The Activity of Synthetic *Lactobacillus cases* Factor (Folic Acid) as an Antipernicious Anemia Substance. I. Observations on Four Patients. Two with Addisonian Pernicious Anemia, One with Nontropical Sprue and One with Pernicious Anemia of Pregnancy. *J Lab & Clin Med* 1945 Dec v 30 No. 12 1056-69 4 figs [30 refs.]

Clinical and hematologic remissions were induced in two patients with Addisonian pernicious anemia by the daily oral administration for ten days of 30 mg and of 100 mg of synthetic *L. cases* factor (folic acid) respectively. One patient with macrocytic anemia of nontropical sprue and one patient with pernicious anemia of pregnancy responded in a similar manner when given daily 20 mg of the preparation intravenously.

Reasons are given for interpreting these results as indicating that *L. cases* factor possesses antipernicious anemia factor activity. It is pointed out however that the material must be proved effective parenterally, in much smaller doses and over a much longer period of time before it can be accepted as being closely similar in action to (or identical with) the effective principle present in liver extracts.

DISCOMBE G. Criteria of Eosinophilia. *Lancet*. 1946, Feb 9 195-6 [12 refs.]

As it became necessary accurately to determine the eosinophil counts of a series of patients and as the limited staff was insufficient to undertake by ordinary methods the large number of differential counts required the possibility of using a simpler and more rapid technique for the determination of eosinophilia was considered.

Although cover-slip films are less subject to errors due to differential distribution of cells than are smears on slides mathematical calculations showed that increases in the proportion or absolute number of cells present to the extent of 1-5 per cent in blood can be detected with certainty by a differential count only if very large numbers of cells are counted in cover-slip preparations. However methods for counting eosinophils in a haemocytometer have been devised and as the uncertainty of such counts varies with the square root of the number of cells counted the error can readily be made as small as desired by counting more cells. The following method was therefore adopted—

Blood is diluted with the fluid (1 per cent aqueous eosin) and acetone 5 volumes each distilled water to 100 volumes (this keeps for some weeks) and after mixing is allowed to stand for 5 minutes. After the pipette has been

shaken vigorously by hand for 2-3 minutes, a Fuchs-Rosenthal chamber is filled and when the cells have settled (1-2 minutes) the preparation is examined with a 2/3 in. objective and a  $\times 10$  eyepiece under the most brilliant illumination tolerable. In such preparations the unstained leucocytes cannot be seen and the eosinophils stand out as deep red particles easily countable. clumping is unusual, but if it develops the preparation must be rejected. Careful investigations showed the method to be entirely satisfactory. For routine work, two pipettes should be filled, and one Fuchs-Rosenthal chamber filled from each. If the whole ruled area (3.2 sq. mm.) is counted and 104 or more eosinophils are found, corresponding to a count of 325 per cmm. it is certain that eosinophilia is present. The normal range of eosinophils is up to 240 per cmm., and not more than 1 per cent. of normal subjects should have counts above this.

It was possible to demonstrate a mild degree of eosinophilia (400-500 per cmm.) in most quiescent asthmatics but the method was principally used in following the treatment of patients with injections of gold salts as it has been shown that toxic manifestations of chrysotherapy are associated with eosinophilia, and as routine differential counts have been recommended for the early detection of this toxicity.

F. Mergatroyd

SIMONET P & GIRARD J. Syndrome de Loeffler à forme macronodulaire chez une asthmatique [Loeffler's Syndrome in an Asthmatic.] *Semaine des Hôpitaux de Paris* 1946 Feb 21 & 22, No 7 283-90 4 figs.

## VENOMS AND ANTIVENENES.

ABUJA M L & BROOKS A G. A Suggested First Aid Treatment for Cobra Bite with Carbolic Soap Solution. *Indian Med Gaz.* 1945 Sept., v 80 No. 9 461-3.

As long ago as 1924 the observation was made that soaps could detoxify snake venoms and CARMICHAEL [this *Bulletin* 1928 v 25 291 and CERARI & BOQUET (*ibid* 1938 v 35 435)] showed that sodium ricinoleate was antitoxic *in vitro* to *Crotalus* and *Liaspis aspis* venoms.

The authors have tested the action of many substances—colloidal metals, dyes, biological products—to ascertain their detoxifying powers against cobra venom in pigeons but all were ineffectual. They then tried various soaps and obtained success with emulsions of Lifebuoy carbolic soap which is to be found in most homes. The soap in 5 per cent. emulsion, infiltrated in doses of 1-2.5 cc. at the site of inoculation of the venom into pigeons of about 300 gm. weight, is effectual against 0.4 mgm. of venom when injected even as late as 1½ hours afterwards. Fourteen survived out of 18 whereas all of 10 untreated died. Even in those which did not survive death was delayed for several hours. This delay would in many cases enable antivenene to be obtained and, in the authors' experiments where the soap was followed by antivenene even as long as two hours later many survived larger doses still of the venom.

The authors give details of the method which they recommend. If a finger is bitten a tourniquet is applied at the base of the finger and another above the elbow. If a toe at the base of the toe and above the knee then the 5 per cent. soap emulsion (which could be kept ready at the local dispensary with a sterile syringe) should be injected, 0.5-1.0 cc. at points surrounding the bite—5 cc. in all could be given—and bleeding encouraged by crucial incisions with a razor blade. Potassium permanganate they regard as valueless and even harmful.

as it may cause sloughing and gangrene. The soap must not be given intravenously and never as a substitute for antivenene. It is purely a *first-aid treatment*.

The authors ask that it may be tried more widely and invite reports especially regarding the following points for information —

- (a) Was the snake definitely identified as a cobra?
- (b) Site and details of bite
- (c) Interval elapsing between bite and injection of soap solution
- (d) Quantity of soap solution injected.
- (e) Antivenene (including period after bite at which serum was given dosage and whether administration was intravenous)
- (f) Other details with regard to local reaction symptoms and progress of the case

H Harold Scott

### DERMATOLOGY AND FUNGUS DISEASES

EPSTEIN E. The Lichen Planus—Eczematoid Dermatitis Complex of the Southwest Pacific. A Study of 65 Cases. *Bull U.S. Army Med Dept* 1945 Dec v 4 No 6 687-94

In an introductory paragraph to this paper Epstein records that when it was written the dermatoses contracted overseas were assuming a major aspect in the disabilities suffered by the armed forces and that those serving in a medical unit which received evacuees from all battle fronts developed a healthy respect for the skin injuring factors in the Southwest Pacific particularly in New Guinea and the adjacent islands. The malady which he names the lichen planus-eczematoid dermatitis complex (known to the troops as jungle rot) was the most frequent cause of evacuation for skin diseases from this area. Of a series of 65 cases exhibiting the malady 34 per cent. were in the 25 to 29 age group and 35 per cent. were older than 35 years of age. The sex incidence was approximately equal race did not seem to be important brunettes were more commonly affected than blondes. Usually the patients had spent three to six months in New Guinea before developing an eruption. The first lesion frequently appeared on an exposed area. Occasionally a generalized oedematous desquamative dermatitis developed in a few days but in most cases from one to three months were required for full efflorescence. The lesions were of three types two of which co-existed in more than half the patients. The first type was an aberrant variety of hypertrophic lichen planus the lesions being purplish, coalescent nodules having smooth scaly warty or pseudo-desquamative surfaces. The face palms and soles were frequently affected. The eruption which might be either localized or generalized did not tend to follow the usual distribution pattern of lichen planus. Sometimes marked atrophy or pseudoatrophy followed the disappearance of the primary lesions. The details in which despite its general appearance the eruption differed from true lichen planus were atypical localization occasional atrophic sequelae abnormal histological features absence of typical lichen planus papules marked pigmentation and frequent transformation into an eczematoid exfoliative dermatitis-like eruption. In the second form the eruption was eczematoid and affected especially the legs hands forearms neck and ears the lesions erythematous-violaceous in colour were flat and covered with branny scales. The underlying skin was often thickened. In the more acute varieties the lesions oozed. The nails showed changes such as those which occur in eczematoid eruptions of the extremities. Sometimes generalized exfoliative dermatitis supervened. The third variety

that the rate of sickness declined. Of 1,500 men, 15 died in 7 months a proportion which compared favourably with the monthly death roll of 60-120 in neighbouring camps. Local purchase of food (rice-polishings and meat) and drugs was allowed—prices were very high.

At this time the main diseases were malaria, beriberi, tropical ulcer and dysentery (amoebic increasing and bacillary decreasing). Shortage of specific drugs presented a difficult problem when it came to deciding to whom they were to be given. Diphtheria occurred but in spite of the fact that no anti-toxin could be obtained there were only two deaths in 20 cases. In some of these cases Vincent's infection was probably also present.

Later the Japanese abolished the weekly half-day rest and the men were given no chance to wash or air their clothes. Scabies ringworm and other skin affections were rife—the huts were heavily infested with bugs and lice scrub typhus, beriberi pellagra, malaria, the dysenteries and tropical ulcers were becoming increasingly common. The Japanese, however began to issue pay to the prisoners who all subscribed to a central pool for purchase of supplementary food and drugs—rice-polishings were bought and issued each day with the result that there was a marked decrease in the incidence of beriberi.

Later the battalion moved into an area in which cholera was prevalent but the men (who were mostly educated) had previously been warned by the author and instructed how best to prevent infection, with the result that only seven died whereas other units lost up to 50 per cent of their strength. The Japanese commander—a non-commissioned officer—refused to permit the organization of a sanitary squad big enough to cope with the situation or to allow water to be drawn from the river above the point at which the coolie labour force contaminated it. The coolies themselves were badly affected by the epidemic and large numbers died—they were allowed no medical attention, and were given neither food nor water except that which the British orderlies surreptitiously passed to them. The dead were buried in pits necessarily dug much too close to the camp because there were not enough men to clear the jungle. [In many other camps the dead were cremated.] The author had already constructed a small plant for the distillation of water for intravenous salines and this form of treatment was used during the outbreak together with the oral administration of potassium permanganate (3 grains every quarter of an hour). In a few cases sulphapyridine was used apparently with good results.

It was not surprising that after months of these appalling conditions, with more or less constant incapacitation from one or several of the prevalent diseases and totally inadequate facilities for treatment the more chronically sick tended to become apathetic and exhausted beyond endurance. [Persuading these men to eat was a continual difficulty.]

L. H. Turner

GHOSH, L. M. & PANJA, D. A Case of Rhinoscleroma. *Indian Med Gaz.* 1945 Oct. v 80 No 10 511 4 figs. on 1 pl.

HARVEY, A. M. KUFFLER, S. W. & TREDWAY, J. B. Peripheral Neuritis. Clinical and Physiological Observations on a Series of Twenty Cases of Unknown Etiology. *Bull Johns Hopkins Hosp.* 1945 Aug. v 77 No 2, 83-103 5 figs. [13 refs.]

The condition described in this paper occurred among men of the United States forces who had served in the tropics. In 16 of the patients the common peroneal nerve was involved, in three the axillary and in one the radial. No known aetiological factor to account for the neuritis could be discovered, and there was no evidence of diphtheria or of vitamin deficiency. In the majority of the patients the condition appeared suddenly the onset being gradual in

only four of the series. In eight of the patients there had been an attack of benign tertian malaria within eight days of the onset of the neuritis two had had malaria at some other time but in the remaining ten patients there was no clinical or laboratory evidence of malaria.

In all cases the patient's complaint was of weakness of an extremity. The three men with axillary nerve involvement and two of the others complained of severe pain. Numbness or paraesthesiae occurred in 14 of the patients. Loss of muscular power was most marked in the patients with axillary nerve lesions all these had complete loss of deltoid function and in two of the three there was evidence of involvement of other nerves of the brachial plexus. Muscular weakness was not so prominent a feature in the patients with peroneal nerve involvement in only three of these was there much atrophy. Laboratory investigations did not help in clarifying the aetiology of the condition.

Electromyographic studies were made on the affected muscles by stimulating the nerve trunk with condenser discharges or an induction coil and recording the action potential in the muscles by cathode ray oscillograph. It was found by this method that the voltage of the action potential of the affected muscles was less than normal. The amount of reduction of voltage was proportional to the muscular weakness as assessed clinically. When a second stimulus was induced at a short interval after the first the affected muscle responded in a manner similar to a normal muscle. There was no evidence of a summation of impulses at the neuromuscular junction. It was thought these facts indicated that the nerve fibres which were affected were completely inactive surviving fibres functioning normally and that there was no defect of muscle fibres. A tetanic stimulation did not produce a myasthenic response nor did prostigmine alter the character of the muscular contraction.

Treatment consisted in rest the prevention of stretching of the affected muscles and graduated exercise. The radial palsy and with one exception the peroneal palsies all improved slowly to satisfactory recovery but the axillary palsies did not recover while under observation. The authors concluded that the neuritis could not be connected with the antimalarial suppressive treatment with quinine and atahrine which all the patients had had. Nor was there any evidence in favour of a vitamin deficiency.

The possible relationship between the condition described and malaria is discussed. The type of neuritis which the authors found in association with malaria presented as polyneuritis with pain and heightened muscle tone whereas the patients in this series complained of weakness in muscles supplied by a single or a few nerves. Pain was not consistent and muscle tone was poor. It is concluded that malaria was not primarily responsible but might have been a precipitating factor. The literature is reviewed and attention is drawn to the reports of similar cases made by SPILLANE and by WYBURN MASON. The paper ends with the case histories of two patients who presented typical signs and symptoms.

[This is yet another report on a series of cases of a type of neuritis which is receiving increasingly more attention in the medical press. One would have welcomed information as to whether any of the patients had received prophylactic or therapeutic serum injections.]

W. Tegner

VAN DEN BERGHE L. Syndrome thrombopénique on onyali. Observation d'un cas provenant du Congo Belge. [Thrombocytopenia, or Onyali, in a Patient in the Belgian Congo.] *Ann Soc Belge de Méd Trop* 1945 June 30 v 25 Nos 1/2 49-55

The importance of this case lies in the facts that the patient was a European and that his history of symptoms prior to those characteristic of onyali were



peculiar. After a journey of three months in the bush the patient in September 1938 complained of feeling tired and consulted a doctor who could find nothing definite. The man therefore continued on his way. Soon afterwards he felt severe pain in the left wrist which became swollen and the following day the right wrist swelled in the same manner. After the application of hot compresses for three days these symptoms disappeared. The right shoulder was then affected but cleared up on similar treatment after a week. Eight days later the left knee swelled and was so painful as to prevent sleep but he continued at work and the condition cleared up in eight days. Some time later he felt discomfort in the teeth and small bullae appeared at the base of the lower incisors. He noticed that he was becoming jaundiced. In January 1939 he complained of dryness of the throat and difficulty in swallowing followed by an acute pharyngitis with marked swelling and for four days he could swallow nothing. Gargles and inhalations gave relief but haemorrhage from the mouth and gums supervened and the jaundice increased. While being examined by the doctor he had a fainting attack followed by coughing or vomiting of blood (it was not decided which). Thereafter he had frequent bleedings from his gums and spat up blood. Slight exertion caused much shortness of breath. He went into hospital towards the end of February and a blood examination yielded the following information: red cells 900 000 leucocytes 3 600 thrombocytes 5 600 per cmm. haemoglobin 77 per cent colour index 1.6 erythroblasts numerous. He was seen by a specialist cardiologist who prescribed salicylates which made him worse. Red cells fell to 600 000 white 2 000 per cmm., haemoglobin 18 per cent. He was then given blood transfusions without much improvement till some 20 had been given when the red cells reached 4 million. More transfusions of 250 cc. were given on alternate days and the red corpuscles rose to 4 700 000 the white cells to 4 600 per cmm. and the haemoglobin to 89 per cent. Thrombocytes now were 80 000. He was kept under observation and was seen every three months for four years and remained well. In 1944 he was killed fighting in the great war.

The causation is considered but no conclusion is arrived at. It is suggested that insect bites might have injected some hypothetical virus or that as on his journeys he often had to push his motorcycle for considerable distances his head would then be near the petrol tank and he may have been poisoned by inhalation of petrol fumes.

H. Harold Scott

SMOURIE K. L. An Outbreak of Lathyrism in Central India. *Indian J Med Res* 1945 Oct. v 33 No 2 239-47 [16 refs.]

The outbreak studied by the author occurred in the eastern part of Bhopal State Central India. At least 1,200 are said to have been attacked. He examined some 150 and studied more closely about half that number. Most of these were in the second and third decades of life and males preponderated over females in a proportion of 7 or 8 to one. Of 69 cases specially noted 56 occurred during the three months August-October the figures being 11, 23 and 22, respectively. There is nothing particular regarding the symptoms: they were typical. Those attacked were of the poorer classes. For the past 2-3 years the crops have been bad and damaged by rust, blight bad weather etc. and the people have mixed cheaper grains in increasing amounts with the wheat, and for some months—six or more—had been consuming large quantities of *Lathyrus sativus*. Examination did not discover any admixture with *Vicia sativa*.

Lathyrus can be consumed in small or even moderate quantity with impunity but when it has to be used almost exclusively for six months or so danger is imminent. The obvious remedies are to provide alternative crops and improve

the condition status and earning power of the agricultural labourer In the words of the author prevention is a social economic administrative and agricultural problem H Harold Scott

MIRSKY C. A Case of Stinkblaar (*Datura stramonium* L.) Poisoning associated with Hyperpyrexia. *Clin Proc Cape Town* 1945 Nov v 4 No. 9 509-12.  
[See this Bulletin 1945 v 42 497 488]

FRACHTMAN H J & MCCOLLUM W T Portuguese Man-of-War Stings Case Report. *Amer J Trop Med* 1945 Nov v 25 No 6 499-500

A sailor aged 23 when swimming was stung on his arms and thighs by a Portuguese man-of-war (the jelly fish *Physalia pelagica*) An hour and a half later he was nauseated and soon afterwards began to have spasms of the abdominal muscles His temperature on admission to hospital was only 98.6°F but the pulse was 96 and respirations 24 per minute and he was very apprehensive. Little or nothing abnormal was discovered by blood examination red corpuscles were 4½ million leucocytes 11 500 per cmm haemoglobin 14.9 gm and the differential leucocyte count normal. Red lines not raised were visible over the front of the right thigh and shoulder In spite of the spasms of the abdominal muscles and diaphragm there was little if any respiratory distress but the muscular contractures became more severe and spread to the neck arms and legs with muscular pain. External stimuli such as bright lights jarring of the bed or sudden noises precipitated the attacks the mind remained clear Ten hours later respiration was slow and laboured, interrupted by diaphragmatic spasms but there was no cyanosis and the temperature pulse and blood pressure were within normal limits [our italics] On the next two days the patient was better in the mornings but the symptoms returned later in the day during the next five days the spasms gradually diminished and on the sixth had ceased altogether and recovery was complete and uninterrupted. [The patient was said to be a well-adjusted individual who had no abnormal psychoneurotic tendencies but he was very apprehensive and the fact of respiratory distress without cyanosis or change in pulse rate is much in favour of a hysterical element being present Nothing is said of the pain and numbness which are usually present in stings by *Physalia* but a choking sensation dysphagia and dyspnoea are common together with spasm of the abdominal muscles This case is perhaps peculiar in the prominence of the last named symptom] H Harold Scott

# GENERAL ENTOMOLOGY

KNIPLING E F The Development and Use of DDT for the Control of Mosquitoes. *J. National Malaria Soc* Tallahassee Fla. 1945 June v 4 No 2 77-92. [23 refs]

At the laboratory of the Bureau of Entomology and Plant Quarantine in Florida U.S.A. investigations into the uses of DDT for mosquito control began in October 1942. In this paper the author briefly summarizes and in some cases discusses a number of the tests made in the laboratory and in the field against larvae and adults of the following anophelines and culicines *Anopheles quadrimaculatus* *Anopheles albimanus* *Anopheles crucians* *Culex quinquefasciatus* [*C. fatigans*] *Aedes aegypti* and *Aedes taeniorhynchus* (234)

wise in the marrow the sharp edge cuts the marrow so that the groove is filled. A cannula fits over the rod in its upper part between the proximal end of the groove and the handle.

The point is made to enter the bone vertically then the handle is depressed to an angle of 30° to the surface of the sternum and the rod is pushed into the marrow for 1 cm. It is then rotated clockwise for one or two turns and withdrawn the cannula preventing the soft tissues from displacing the marrow from the groove. Satisfactory smears can be made, the cell counts being more accurate than in smears of marrow obtained by aspiration where dilution with blood occurs [see also MERTENS this *Bulletin* 1946 v 43 257]

J F Corson

SUÁREZ R. M. DÍAZ RIVERA R. S. & HERNÁNDEZ MORALES F. Hematological Studies in Normal Rhesus Monkeys (*Macaca mulatta*). 1. Venous Blood Studies. 2. Bone Marrow Studies. *Puerto Rico J. Pub. Health & Trop. Med.* 1942, Dec. v 18 No 2, 212-26 1 pl. [Refs. in footnotes.] [Spanish version 227-41.]

Being struck by the scarcity of publications dealing with the cell content of normal monkey blood and the complete lack of information regarding the cells of the bone marrow the authors decided to study the blood and bone marrow in normal rhesus monkeys of various ages. The blood was obtained from a peripheral vein in 38 while the bone-marrow was aspirated from the sternum of 40. The general results of the study of this material are given in the summary to the paper which is as follows —

"1 Hemoglobin estimations for 38 Rhesus monkeys were as follows: infant monkeys 84-82 per cent. young 90.5 per cent. adult, 91.16 per cent., with ranges of 76 to 94 80 to 110 and 76 to 117 per cent. respectively.

"2. Red blood cell count averaged 4,197,500 in the infant 5,172,500 in the young, and 5,235,000 in the adult animal.

"3 Platelet count averaged over 300,000.

"4 Reticulocyte counts were 2.9 per cent. for infant, 1.85 per cent. for young and 1.58 per cent. for the adult animals.

"5 The average total leukocyte count was 15,107 for infant 17,562 for young and 9,999 for the adult animals.

"6 Metamyelocytes averaged 0.75 per cent. in the infant, 0.5 in the young and 1.15 in the adult animals.

"7 Neutrophils were more abundant in the venous blood of the adult than in that of the young or infant monkeys: the average for the infant being 36-12 per cent., for the young, 33 per cent. and for the adult 50-25 per cent.

"8. Eosinophilia was quite pronounced in the young and adult monkeys which may be attributed to intestinal parasitism. Averages of 3.08 were found for infant animals 4 per cent. for young and 4.02 for adult.

"9 Lymphocytes were found in higher percentages in both infant and young animals than in adult, such percentages being above 40 in all the series analyzed. Averages were given of 57.75 for the infant, 58.75 for the young, and 42.19 for the adult animals.

"10 It was the authors' impression that there is a relative proportion of different blood elements in the monkey comparable to those of the human infant and young however these differed slightly from the venous blood of the adult human.

"11 Morphologically the neutrophils and eosinophils appeared to have multiple lobulations in their nuclei sometimes as many as thirteen to fourteen lobes were counted in one cell. The lymphocytes appeared to be larger than in human blood and, in many cases coarsely granulated.

The following results were obtained among the forty *Macacus* submitted to bone marrow aspirations

1 The average erythrocytic series in the infant was higher than in either the young or the adult animal

2 The average granulocytic series was higher in the adult than in either the infant or young the young animal's marrow being richer in those cells than the infant's

3 The young monkey had more erythrocytic cells in its marrow than the adult.

4 Lymphocytes were more numerous in the infant and the young than in the adult monkey

5 Ratios for erythrocytic and granulocytic components were as follows  
infant 1 2.8 young 1 3 adult 1 4

6 Morphologically, the cells of the bone marrow resembled those of humans except for the multiple lobulations of the nuclei of the polymorphonuclear leukocytes and for the larger size of the lymphocytes of the animal.

7 Megakaryocytes were seen in very low percentages 0.2 in only two adult animals. None were seen in either young or infant monkeys

8 If it were not for the high number of lymphocytes the bone marrow of the monkey would approach the human picture at different life stages.

C M WENYON

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## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

WENYON C. M. *Tropical Medicine in War and Peace. Trans Roy Soc Trop Med & Hyg* 1945 Dec. v 39 No 3 178-94

This presidential address refers to the stimulus provided by the two world wars to research into the possibilities of improving methods of safeguarding the health of troops in tropical and sub-tropical countries. Very noteworthy contributions to tropical medicine were made in both. During the 1914-18 war LEIPER worked out the life-history of *Schistosoma haematobium* and *S. mansoni*. Important additions to our knowledge of the dysenteries were made. Weil's disease was intensively studied. The louse was incriminated as the vector of European typhus fever and the Weil-Felix reaction was elaborated. The limitations of quinine in the treatment of malaria were more clearly defined as a result of war experience.

The second world war has been even more productive of new knowledge than the first. Most important of all perhaps is the knowledge of what atabrin can do to prevent clinical malaria among troops operating in hyperendemic malaria country. The important work of FAIRLEY and his colleagues at Cairns in Australia is strongly suggestive of the existence of an exoerythrocytic cycle of development of the human malaria parasite. The discovery of the remarkable insecticidal properties of DDT is of great and far-reaching importance. Insect repellents have been discovered—dimethyl dlethyl, and dibutyl phthalates—which do what is claimed for them. A vaccine against scrub-typhus (*tsutsugamushi* disease) has been prepared and used, but the results have not yet been reported. Against louse-borne typhus a formalinized rickettsial vaccine prepared from egg yolk cultures has been widely used and it is believed that some degree of protection was afforded, but DDT has given the most remarkable results in the prevention of typhus fever. A shirt impregnated with DDT retains its insecticidal properties throughout a number of launderings. In the treatment of bacillary dysentery sulphaguanidine has

been used with most satisfactory results and it is possible that other sulphonamides may be even more effective. In amoebic dysentery cases that are resistant to anti-amoebic remedies marked clinical improvement may follow the administration of penicillin but without eliminating amoebae after this improvement the amoebic infection may become amenable to specific treatment. The war years also saw the final proof that kala azar in India is transmitted by *Phlebotomus argentipes*. Russian investigations in Middle Asia showed that a gerbil, *Rhombomys opimus* is the reservoir of the leishmania of oriental sore which is transmitted to man by *Phlebotomus papatasi* another sandfly *P. caucasicus* being responsible for maintaining the rodent infection in the burrows. Such are the outstanding achievements of tropical medicine during these last war years.

The address then dealt with the future of tropical medicine and with the present state of tropical medicine in Great Britain. At present the facilities for giving instruction in tropical medicine in London, as well as for the study of tropical diseases and their treatment are sadly deficient. A very strong case is made out for the early creation in London the centre of an Empire with vast tropical responsibilities of a Tropical Medicine Centre which would combine a hospital for tropical diseases and a school of tropical medicine. This "would restore the position formerly held by this country would be a monument to the many pioneers who devoted themselves to the study of tropical disease and would be a centre of tropical medical activity worthy of the British Empire."

Norman White

- i. ALLAN P. The Progress of Public Health Work in the Native Territories. *South African Med J* 1945 Nov 10 v 19 No 21 402.
- ii. MEARS, A. R. R. The Part Time District Surgeon in the Transkeian Territories. *Ibid.* 402-3.
- iii. DE VILLIERS, V. M. Rehabilitation of the Transkei. *Ibid.* 405-6
- iv. HUBBARD C. S. Afforestation and Fuel Supply in relation to Development in the Transkeian Territories. *Ibid.* 407-8.
- v. DREWE, F. Some of the Problems of Leprosy. *Ibid.* 408-10 [11 refs.]
- vi. FRASER SHEARER, W. Transkeian Memories. *Ibid.* 410-12.
- vii. SOUTH AFRICAN MED J 1945 Nov 10 v 19 No 21 412-14 Educational Aspects of the National Feeding Scheme.
- viii. ZONDO W. T. The Training of Bantu Women Community Workers at the Mbita Training Centre, Tsolo. *South African Med J* 1945 Nov 10 v 19 No. 21 414
- ix. SOUTH AFRICAN MED J 1945 Nov 10 v 19 No 21 415-17 1 map. Medical Services Transkeian Territories, 1945.
- x. SOUTH AFRICAN MED J 1945 Nov 10 v 19 No. 21 418. Vacation Courses for Medical Students in the Transkei.
- xi. ELDER, J. H. Jeanes Teachers. *South African Med J* 1945 Nov 10 v 19 No. 21 419-20

1. In the introduction to this series of papers Allan remarks that there is now much more movement into and out of the Native Territories of South Africa than was the case 25 years ago and that this movement has entailed much spread of disease and much change in mode of life. During the last 4 years a concerted attempt has been made to deal with these diseases, and the work will be continued.

ii. The paper by Mears is largely concerned with the official duties and private practice of the District Surgeons. He discusses certain grievances but from the point of view of readers of this *Bulletin* the important part of the paper is that in which it is stated that in the Transkei there are 1,281,823

Africans 17,598 Europeans and 10 000 Coloured for this population there are 13 hospitals (8 of which are mission hospitals) with 607 beds and about 50 doctors.

vi. De Villiers refers to the basic reasons for the deterioration of agriculture and health in the Transkei which for many years has been a matter for concern. The land has become seriously eroded and denuded as a result of over stocking and inefficient farming there has been a steady deterioration in the quality of cattle and a shortage of milk for human consumption. The result has been serious malnutrition and heavy infant mortality. [The general position was set out in the series of papers reviewed in this *Bulletin* 1943 v 40 865.] Plans have now been made and work started to improve the general agricultural position. The project is very big but not too big for the problem it entails much engineering construction work afforestation agricultural supervision and education and introduction of new stock with restriction of the old. It is a programme which will affect health chiefly because it is directed against the fundamental causes of ill-health malnutrition and ignorance. Already a useful amount of work has been done.

iv. Hubbard takes up the subject of afforestation and fuel supply showing that at present the wood taken for fuel is much below even a reasonable minimum yet because this wood is scarce the people burn farm manure and mealie stalks which are needed to fertilize the land. Moreover timber is an essential for construction purposes in any health or industrial programme. The proper degree of afforestation is therefore important for health and the balance between the use of land for this purpose and for agriculture must be worked out with care.

v. Drewe discusses leprosy as he has seen it at the Holy Cross Mission Hospital. Many of his points have already been noticed in this *Bulletin* 1945 v 42 292.

vi. The paper by Fraser Shearer is well described by its title those who have practised surgery in Africa will recall cases similar to those he describes of the immense resistance to shock and infection exhibited by the Africans. He makes one point of public health importance, however in his remarks on the senile patient with chronic pulmonary tuberculosis and positive sputum who lives with his family during his slow decline and infects the younger members. If we trouble to elicit his family history we find in 80 per cent of cases that the patient's children and even grandchildren have died in numbers in their early teens of acute miliary tuberculosis. The building of hospitals for the acute cases in contacts seems futile while the source of infection is allowed to remain at home and to continue to infect others. The author suggests some form of segregation on farm colony lines for these chronic cases.

vii. The author of this paper Mr J H Dugard is an Inspector of Schools but he writes with authority for the administration of school feeding has been delegated to the Education Department. He points out that there is an obvious correlation between low income and malnutrition but also that ignorance of dietary factors often produces malnutrition even when the income is satisfactory. In most families in the Transkei the schoolchildren receive only one meal each day—on their return from school—and such children are suffering from starvation not mere malnutrition. It is to provide such children with enough food to prevent starvation that school meals are arranged. The author remarks that in the interest of national welfare collective action to prevent human deterioration is necessary by means of a well-designed feeding scheme for children. [National welfare is of course important but it would fit in with the ideals of medical men if equal stress were laid on the fact that starvation or any other adverse condition must be prevented in the interest of the child as an individual who is not responsible for his own environment.]

and who should not therefore be penalized for it.] School-feeding is still in the experimental stage in South Africa, and the composition of the meals is not always good. The allowance of 2d. per meal is not ungenerous and at that price the diet designed by Dr S. KARK at Polela is good, but there is in some places too great a tendency to supply bread and jam, condensed milk, pork of dubious quality and mealie-meal with monotonous regularity instead of making determined attempts to procure protective foods. School meals should be regarded as breakfasts and should be given as early in the day as possible.

vin. The training to which the author refers consists of one year during which time women of approved capacity are given instruction in domestic, agricultural and medical subjects before they go to work among the African communities.

ix. In a table of facts about the Transkei it is stated, among other things that between 80 000 and 100,000 Natives leave the Transkei each year to seek work on the mines or in other industrial centres. 28 per cent. of families have neither cattle nor land. Smallpox was prevalent during 1945 but typhus was less in evidence than during 1944 perhaps because the outbreak of that year left a residual immunity. Approximately 100-200 persons with tuberculosis are repatriated from the mines each year.

x. This short note contains the outline of a most excellent plan by which students from the Medical Schools of the Union are given the opportunity of seeing for themselves the work carried out in the Native territories. They are introduced to the relationship of the soil to medical practice, of the place of afforestation in the health and welfare of the people, of the relative value of pamphlets and posters and the cinema in the education of the public, and why people leave the land to seek employment in overcrowded industrial areas.

xi. Miss Ekler, the head of the Jeanes Teachers Training School All Saints Mission, gives a short account of the function and training of these African teachers in which she refers to the Jeanes School at Kabete in Kenya. Their name derives from Miss Jeanes, a Quaker lady of the United States, who founded the movement in the interest of better education for the Negroes. The object of these teachers is to widen the scope of school education to include training in practical domestic science, market gardening and small farming with instruction in hygiene, elementary nursing and cooking. The evidence all points to the need for such teaching among the Africans, and to the success of the efforts so far made, but she adds — It seems the greatest pity that the training of these teachers has now come to an end in the Cape Province and has never been started anywhere else in the Union for now is the time when a steady stream of such people joining the flood of workers that will be needed to rehabilitate the Transkei in the critical years to come might make a most valuable contribution to their country's welfare. A reader is left to wonder why the training of Jeanes teachers has been abandoned.

[This series of papers is important in that it gives the reader a picture of life at almost its lowest level in the people of South Africa, and in that it shows the field from which the impetus for improvement should arise. Medical men and social workers see as clearly as any others the ultimate effects of policies adopted by central governments and it is part of their duty to make the necessary representations to governments so that these policies can be modified where change is needed. The papers also demonstrate the obvious fact that good health depends upon agriculture and education no less than on strictly medical activities. These facts are appreciated by the Government of South Africa, and if the recommendations made in the *Report of the National Health Services Commission* (U.G. No. 30-1944) are put into effect there is every reason to believe that the situation will be radically altered for the better.]

This Commission set out comprehensive schemes for personal health services (promotive preventive curative and rehabilitative) and non personal health services with the object of applying them to all sections of the population according to their need and without regard to race colour means or station in life. No brief account of this long report is possible it is an admirable document which would serve as a basis for any scheme for comprehensive medical service in Africa and it should be studied in detail. The authors recognize the importance of agriculture to health but think that the function of a national health service in this respect is to advise but not itself to embark upon the provision of food. The report states that the long term policy with regard to nutrition is obviously to improve purchasing power. Consideration of this however would lead to a very complicated discussion of socio-economic problems beyond our terms of reference. The short term policy essential on health grounds should be to extend the activities already in operation especially in respect of protective foods and to subsidize consumption by low income groups particularly expectant mothers and pre-school children within these groups. An account of the substance of this report is given by A. R. PATERSON in the *East African Medical Journal* 1945 July v 22 No 7 204.]  
Charles Walcock

COLCHESTER T. R. Social Services for Africans in the Nairobi Municipality, Kenya  
*Oversea Education* H.M. Stationery Office 1948 Jan. v 17 No 2, 254-6

SCHUFFNER, W. Organisation der Bekämpfung der Tropenkrankheiten in Niederländisch Indien. [Organization of the Campaign against Tropical Diseases in the Netherlands East Indies.] Reprinted from *Ein Querschnitt durch die neueste Medizin dargestellt von ihren Schöpfern* (ADAM C. Editor) *Veröffentlichungen d. Berliner Akademie f. ärztl. Fortbild.* 1940 No 6 145-64 16 figs

ORENEY, Jean M. The Health of Indian Women and Children. *J. Ass. Med. Women in India* 1944 Feb. v 32 No 1 5-16

The author who is exceptionally well qualified to deal with the subject shows that the standards of health of Indian women and children are even lower than those of the population as a whole.

A few figures will suffice to illustrate the distressing wastage of life and health that still occurs. Corresponding figures for females in England and Wales are shown in brackets.

The expectation of life for Indian females in 1930 was 26.58 years (62-67 in 1931). The specific death rate for females in British India in 1930-32 at the ages 15-19 was 10.6 (2.3) and at the ages 20-29 it was 11.9 (2.9).

The maternal mortality rate for India is not accurately known it is estimated as 15-20 (2.76 in 1941). The wastage of life is most pronounced in early life of all the deaths occurring in British India the percentage among children under ten years is 48.5 (10).

The causes of the low level of health of women and children are discussed under the heading of social security education and organized public health. Details are given to show how utterly inadequate is the supply of medical women and health workers and a plea is made for the extended use of instruction in hygiene among teachers and schoolchildren.

A brief reference is made to the population problem it is stated that "A continuous adjustment between the population and the resources available will be needed and constructive thought must be given to the means of making these adjustments but no suggestion is made for the inclusion of the subject in the sphere of action of the public health department."



In a nutritional survey in an urban area at least 38 per cent. of the mothers were found to be malnourished and in a group of 284 infants 168 under the age of six months were in a good state of nutrition but when they had reached the age of one year only 31 could be placed in this category

John W. D. Megaw

UNITED STATES NAVY BUREAU OF MEDICINE & SURGERY. *Epidemiology of Diseases of Military Importance in the Netherlands Indies, including the Identification and Distribution of Arthropods of Medical Importance.* [Navmed 133.] pp. vi+250, 19 figs. (maps) & 1 pl. [Bibliography] 1944 Washington U.S. Govt. Printing Office. [40 cents.]

GUXX D. L. KIRK, R. L. & WATERHOUSE, J. A. H. An Improved Radiation Integrator for Biological Use. *J. Exper. Biol.* 1945 Dec., v 22 Nos. 1/2, 1-7 3 figs. [10 refs.]

The authors describe laboratory work with radiation integrators which are instruments designed to sum up the amount of radiant heat received over a period.

A good many years ago Buxton was engaged on the study of climate in relation to insects. It was well known that radiation of many wave lengths is of very great biological importance but difficult to measure by any existing apparatus. He endeavoured to produce a relatively simple instrument and was prepared to be content with a relative figure even if it had been impossible to reduce the readings to some such units as gram-calories per unit of area and time. He produced an instrument which consisted essentially of a black bulb in vacuo full of a volatile liquid and exposed to the sun. It was connected to a burette which was at shade temperature. Radiant heat from the sun falling on the black bulb heated it and caused the liquid to distil from the bulb into the burette. With this instrument he showed that there were large seasonal differences in the amount of radiant heat received at different seasons in the Samoan islands—these differences were not shown by shade temperature owing to the thermostatic effect of the surrounding ocean.

The present authors have had the use of Buxton's original apparatus and have evolved improved types which can be made in a more nearly standardized manner. They have calibrated these instruments in the laboratory with a source of radiant heat and a pyrheliometer and they have developed the theory and made some approach towards obtaining absolute measurements.

An apparatus of this type has the advantage that one can control its sensitivity by altering the volatile liquid. The present authors find that if the instrument is exhausted and filled with water the amount of distillate is relatively small, so that the instrument can be read once a day to give a mean daily intensity of sunshine. If it is filled with alcohol, which is much more volatile it will give a measure of differences of intensity over much shorter periods.

It seems evident that radiant heat is an important and neglected element of climate. And it seems that this instrument is a simple one which could be set up and used in almost any meteorological station. We look forward to hearing results from tropical Africa, which these authors will shortly be publishing.

P. A. Buxton

## BOOK REVIEWS

MONTEL, M. L. R. *Memento thérapeutique du praticien colonial*. [A Tropical Practitioner's Guide to Treatment.] 118 pp 1945 Paris Masson et Cie  
 Editeurs 120 Boulevard Saint-Germain. [100 fr]

The author of this book has had nearly 40 years experience of practice in the tropics and he holds the position of Medical Officer in charge of the Saigon Polyclinic where more than a thousand patients daily present themselves for treatment. Therefore as Professor Brumpt says in his prefatory note no one is better qualified to write a work on colonial medical practice. The author claims that this work is a concise précis of therapeutics for colonial practitioners. He has intentionally omitted all history and discussion of the mode of action of medicaments and has made choice of such drugs only as he has found efficacious omitting also all references to the literature. In his introduction he states The colonial practitioner finds himself nearly every day confronted with emergencies and his intervention must be active energetic and prompt he ends by saying that this work is a résumé as complete as possible of the colonial practitioner's therapeutic armamentarium. These are very definite claims and it is only right that we should test them and see how far they are made good for a pocket manual if it is to serve its purpose of an aid in emergency must be accurate and precise in its information and is none the worse for being to a certain degree dogmatic.

It is to be feared that those who expect all this will be disappointed. There is much that is good but often the information which will be looked for is too vague to be of any help in emergency. Let us mention the good points first. The information is precise and helpful on the following subjects dysentery both amoebic and bacillary (though not many British practitioners will endorse the opinion that three pastilles a day of dysentery vaccine *per os* for three days are of much benefit in bacillary dysentery) ankylostomiasis schistosomiasis kala azar leprosy (though it is news to the reviewer that enuresis in infants should make one suspect leprosy) opium poisoning malaria (an excellent summary) sprue (but undue stress is laid on the action or failure of action of the pancreas) tetanus tinea imbricata and African trypanosomiasis. Next to justify our statement that the information is often too vague to be helpful we may cite the following *Actinomycosis* Sulphonamides dapsone thiazamide as adjuvant to the classical treatment. One is then referred to Blastomycosis and finds iodine internally and externally auto- and hetero-vaccines by injection by ingestion on dressings brewer's yeast penicillin. A mere list such as this without a word as regards dosage is not of much service. Agam under Yaws I use bivalent muthanol and quinby alone or together with sulpharsenol, acetylarsenol and stovarsol nothing as to dosage or mode of administration. Under *Strongyloidosis* again merely a list thymol ethereal extract of *Filix mas* chenopodium may be tried and quinaquine stannoxyl, gentian violet methylene blue by mouth or intravenously arsenobenzene intravenously and antimonials. Many more examples of this vagueness might be cited but these will suffice.

*Insolation* is very poor nothing is said of the various forms of heat trauma and their different treatments. *Xerophthalmia* is dealt with in three lines under the complications of malaria. The author mentions that in *dengue* there occurs a swelling of the kidneys to such a degree that it is perceptible by renal ballotment and may even lead to the possibility of operation being undertaken for renal tumour. *Rabies* is not referred to at all. There are a number of misprints among them D D T and D T T are used impartially. The subjects are dealt with in alphabetical order so there is no pressing need for an index but it will be gathered from what has been said that the work is

difficult to place and, in spite of its good points the defects are such that in its present condition it cannot be unreservedly recommended as meeting the needs of the tropical practitioner

H Harold Scott.

GHOSE Birendra Nath (M.B.E. F.R.F.P. & S. (Glasg.) F.R.S. (Edm.) etc.]  
*A Treatise on Hygiene and Public Health with special reference to the Tropics.*  
 Eleventh Edition pp xvi+707 161 figs. 1945 Calcutta Scientific Publishing Co. [Rs. 12/8 or 21s.] [Review appears also in *Bulletin of Hygiene*]

Thus the eleventh edition of Ghose's *Treatise on Hygiene and Public Health* appears in less than two years after its predecessor—an interval shorter than that between any two previous editions. We do not know of course the size of the editions but the fact alone bears witness to the popularity of the work. Its merits have been repeatedly extolled in reviews of earlier editions in this *Bulletin* so there is little to add now. The issue of eleven editions in less than 33 years is recommendation enough of its usefulness to public health officials to teachers and pupils alike. The work purports to have special reference to the tropics but only a very small part—in particular the appendices and a chapter on Diet in India—is not applicable to temperate climates equally. In short most of the work is of general application, though the tropical aspect is kept in view.

There are two additional chapters in the new edition one on Camp sanitation—a short chapter but all the essential points are dealt with, such as choice of site the general lay-out of the camp the securing of a safe and ample water supply and the questions of food and cooking and disposal of refuse. The second addition is a chapter on Social Medicine, written by Dr J B Grant, Director of the All-India Institute of Hygiene and Public Health, to whom due acknowledgment is made in the preface.

In a book so excellent and in which so much is included, it comes as a surprise not to find any mention of manganese among industrial poisons, considering the number of important papers on the subject which have appeared in the last five or six years also in work having special reference to the tropics one would expect to see some account of infantile beriberi (which is not the same as beriberi in infants) and of Dr Fehly's work in this connexion. Another disease one misses is sprue and one looks in vain for something about human cysticercosis and hydatid. In fact the only remarks on *Echinococcus* are the brief statement on slaughter-house rules that "Dogs and rats should not be allowed

and the slaughterhouse on account of the danger of trichinosis and echinococcus disease." (p. 102) and "Echinococcus granulosus is found in the cystic or intermediate stage in the liver and other parts" (p. 415). Under venereal diseases nothing is said of lymphogranuloma inguinale or granuloma venereum or of bejel. No mention is made of the association between herpes and varicella.

So much for omissions—one or two mistakes call for rectification. The Black Death did not occur in the 11th century (p. 484) but in the 14th (as stated correctly later p. 499) the discoverer of *T. cruzi* was not Chaga. If the author has any grounds for perpetuating in edition after edition that "a second attack [of yellow fever] within two years is not uncommon," he ought to produce evidence for a statement totally at variance with the views of those who have had extensive experience of this disease.

Finally a suggestion. It would be a great help to students if the degree of magnification was stated of the worms and insects depicted. From the illustrations one would gather that *Gastrophilus hominis* is much larger than *Fasciolopsis buski* instead of being one-fourth the length, and *Fasciola hepatica*

is depicted as being several times as large as *Fasciolopsis buski*. Among the insects the house-fly is depicted as being larger than *Stomoxys* while *Simulium* insects the house-fly is depicted as being larger than *Stomoxys* while *Simulium* *Stomoxys* and the tsetse fly are all about the same size.

All these are points which could easily be put right and the book remains one to be heartily recommended and in these days of expensive books is remarkably cheap.

H. Harold Scott

MOLL, Aristides A. [Ph D Secretary Editor of the Pan American Sanitary Bureau Washington D C etc.] *Aesculapian in Latin America* pp vii+639 numerous illustrations 1944 Philadelphia & London W B Saunders Co [\$7]

As Secretary Editor of the Pan American Sanitary Bureau Washington the author has access to the best medical libraries in the world and he has utilized his opportunities to produce a work of the utmost one might justly say of unique interest. Interesting books may be said to belong to one of three categories (1) Those which may be read continuously from start to finish and which hold one's attention and interest to the end. Often their permanent effect is slight and the work is soon forgotten. (2) Those which produce a more permanent impression and which we turn to and read again more slowly and with greater attention. (3) Those to which we may have to refer in the future and therefore keep always at hand.

The present work by Professor Moll is if not unique very exceptional for it partakes of the characters of more than one of these categories perhaps of all three. To review it really adequately would occupy a whole issue of this *Bulletin* and mere enumeration of the titles of its 78 chapters would fill all the space available for review. We can therefore only touch upon a very few points and otherwise speak in general terms.

The author has dealt with this colossal subject in two main divisions. In the first he writes of times up to the end of the 18th century and in the second from this to the present day. Few people are aware of the richness of the New World in vegetal medicinal plants among them to name only a proportion are *cannabis indica* *carpotroche* *cascara sagrada* *chenopodium coca* *guaiacum* *ipocuanha* *jaborandi* *jalap* *krameria* *sarsaparilla*, and above all *cinchona* and there is little doubt that the American natives were well acquainted with the uses of many of them, their toxic properties their use as diaphoretics as cathartics emetics haemostatics and laxatives. They practised bleeding administered enemata applied poultices made splints of plaster and gums and performed trephining amputations and other surgical operations. Enlightenment had advanced even to the stage of euthanasia for incurables—though euthanasia would seem to be a euphemistic term and a more merciful method might have been found than breaking the back of the unfortunate patient. Cortés had so high an opinion of the skill of native doctors that in a letter to King Charles V he stated that there was no need to send out doctors from Spain. It was thought by many that disease could be got rid of by passing it on to someone else an idea which prevailed in England at least as late as the beginning of the present century when it was a common belief among men with gonorrhoea that they would be cured by passing the infection on to some unsuspecting virgin. It is said that Averroes in 1553 described the circulation of the blood and that Servet (1535) Lobera (1542) Valdés de la Plata (1545) Montaña (1551) and others were also precursors of Harvey and González wrote on *bubas* (yaws) in 1526.

In public health also they went far. The rulers of the Incas made provision at public expense for relief of the poor for cripples for the blind and the aged and in 1524 an ordinance by Cortés required human waste products to be

removed from houses and streets to be cleaned—discharge of domestic waters into the streets was forbidden and all slaughtering of animals had to be done outside the cities. As long ago as 1513 persons were appointed in Porto Rico and Santo Domingo to keep records of births and deaths. After these general matters the author passes on to autochthonous diseases epidemics quarantine, early medical practice and hospitals.

In the second part, designated The Independence Period the author discourses of the developments in medicine and surgery and their various branches and the teaching of them—botany pharmacy dentistry paediatrics, obstetrics, public health, and the rest. A chapter all too short is devoted to medical martyrs many of whom died as a result of attending cases of typhus and yellow fever—the story of Oroja fever *Verruga peruviana*, and Carrón's tragic death is included. The whole work is embellished by numerous illustrations and portraits. There are two invaluable Appendices—one a chronology of disease, taking each in turn—the second a medical and general chronology for Latin America from 1492 to 1943. There is an abbreviated selective bibliography and there are indexes of names and of subjects.

There are two things which detract somewhat from the great value of this work. First, over-condensation in attempting to get so vast an amount of information into so small a space has resulted in the narrative becoming at times little more than a catalogue of names whole pages here and there consisting solely of names and dates. Second, the irritating interposition of foot notes on almost every page, whereby the continuity of reading is repeatedly interrupted. Delightful though the book is it would be even more readable if the information were less condensed and the footnotes were incorporated in the text. Perhaps it is not too late to urge the author—for fresh editions are certain to be called for soon—to divide the work into two or even more volumes. There is sufficient material for half a dozen at least, each as large as this one reading would be facilitated and the information would be more easily absorbed if accounts were fuller for nearly all the chapters could be much amplified with advantage. Interest would be still further enhanced if more detailed biographies were given of some of the hundreds of persons referred to in the text as men of note.

These are just suggestions and do not detract from the great debt which medical practitioners in the tropics and medical historians everywhere owe to the author for this splendid piece of work.

*H. Harold Scott*

RAIG Charles Franklin [M.D., M.A. (Hon.) F.A.C.S. F.A.C.P. Colonel, U.S. Army (retd.) D.S.M. etc.] & FAUST Ernest Carroll [M.A., Ph.D., etc.]. *Clinical Parasitology* 4th Edition, thoroughly revised. 871 pp., 305 engravings & 4 coloured pls. 1945 London Henry Kimpton, 25 Bloomsbury Way W.C.1 [50s.]

The fourth edition of this now famous book is bigger than its predecessor by 104 pages yet it remains a handy volume. The print is the same as before, the paper is good, and the illustrations excellent. Apart from additions in the general text, there is a new chapter on the geographical distribution of parasitic infections and in relation to each important parasite there is a separate section on pathogenesis which is a new feature. The book, of course is more than a treatise on the morphology and life-history of the parasites it contains as before, information on the pathology of the relevant human diseases, their symptomatology treatment and control. During the war much new information has been acquired on the subjects with which the authors deal, and in most important respects this new information has been incorporated if it was

available in time. The authors have been closely associated with the teaching of these subjects during the war and have evidently been alert to receive new information.

For instance, the dry and moist forms of oriental sore recently described in Russia, are mentioned. Bull's fever and Colorado tick fever are described. The use of DDT for many purposes and the trials of hyper immune rabbit serum in the treatment of Rocky Mountain spotted fever and of *p*-aminobenzoic acid for typhus are referred to adequately in so far as information was available at the time when the manuscript must have been sent to press. The sections on African trypanosomiasis and *Glossina* however could be improved. The descriptions of the haunts and habits of the various species of tsetse flies and of methods of control are inadequate. The importance of *G. tackinoides* and *G. submorsitans* in transmission and the difference in the control methods for the river-haunting and the non river haunting species are by no means sufficiently stressed. There is no clear statement of the fact that infections with what is usually regarded as *Trypanosoma gambiense* may be as acute as those due to *T. rhodesiense*. Is the remark that *T. gambiense* may be transmitted by coitus worth retaining?

The section on the vectors of malaria is good now that *Anopheles punctulatus punctulatus* has been added all the important species have been included with the exception of *A. melas* but the breeding places of *A. gambiae* (as stated in the table on pp 642-645) give a poor picture of the habits of this mosquito. The vectors of yellow fever are well recorded and in fact throughout the book the lists of vectors and intermediate hosts are very comprehensive. Two small points (page 371) may be mentioned, *Mansonioides longipalpis* and *M. annulipes* are synonyms and the water plant is *Pistia stratiotes* not *stratioides*.

*Clinical Parasitology* is to be recommended as a reference book and as a textbook to teachers research workers and students alike. It is of the very highest quality.

Charles Wilcocks

BIESHEUVEL S (M.A.(Cape Town) Ph.D (Edin)) *African Intelligence* pp viii+225 12 figs. 1943 Johannesburg South African Institute of Race Relations P O Box 96 [7s 6d]

The title of this book is a sufficient indication of the importance of the subject with which it deals. Whether we start with certain prepossessions about the intelligence of the Africans or with none at all we must admit that as an academic, and as a practical issue it is one of the most important of our day. It should be noted at once that African in this sense means only Africans in the Union of South Africa. No other Africans are referred to in this study and readers who know other parts of Africa have to be constantly checking their reactions to some of the statements and reminding themselves that this is a study in a strictly limited field.

The book originated, as the author explains in his preface from an attempt to review a monograph by Dr L. Fick of the South African Council for Educational and Social Research on 'The Educability of the South African Native'. Fick's main contention was that the mental age of the Africans in the Union was from 4-5 years below that of the Europeans and that the observed inferiority was permanent and innate and not due to preventable environmental influences. Dr Biesheuvel found that a critical examination of this monograph raised so many issues that he had to deal systematically with each problem. Hence his review grew into a book which has all the freshness and drive of a challenge and yet has preserved an essential scientific objectivity. He achieves this by relegating to his final chapter any detailed analysis of Fick's work and by concentrating all the rest of his book on an examination

of the issues involved in comparisons of intelligence on an inter racial basis. It is unfortunate that there is no index to this otherwise well-documented work.

In a brief survey of the leading authorities on the nature of intelligence he lays down as an essential preliminary that "any study of African intelligence particularly if the comparison with the intelligence of Europeans is its chief object, will have to make some choice between the different theories of intelligence now in the field. Arising out of this as a starting point he asserts that intelligence test scores are on the whole of less importance than mental processes and their attributes and antecedents. Two practical issues are then stated, which recur in different forms throughout the book, and which are of far wider import than their occurrence in the Union of South Africa—the formulation of educational policies for Africans and the adjustment of Africans to and their future development in western civilization.

The main chapters of the book fall into two parts. The first deals with the measurement of intelligence the problems of sampling the effect of the cultural milieu on test-intelligence and the suitability of existing tests for measuring African intelligence. The second half reviews the factors of home environment school and nutrition in their effect on intelligence.

In the earlier chapters there are two leading scientific problems which are of wide interest. The first is the question what do intelligence tests measure? Dr Biesheuvel's answer is "We are compelled, therefore to look upon an intelligence test score not as a direct measure of innate ability but as a measure of hereditary potentiality as it happens to have been realized by specific environmental circumstances. The latter half of the book is from this point of view an examination of selected environmental circumstances analysing their effect on the growth of intelligence. The second main problem is that of the control group. Dr Biesheuvel considers that in previous inter racial intelligence studies in South Africa control groups have been chosen where the factors of nutrition and home and school environment have not been equalized. He raises indeed the question of whether the environmental differences are not so great between Africans and Europeans in the Union that the matching of two representative and parallel groups is impossible. He shows how difficult it is to select representative samples of the African population which cannot be done with any accuracy on a basis of division into urban and rural, tribal and detribalized. He discusses such difficulties as the unfamiliarity of the Africans with the test situation and the speed factor in the tests which is based on a peculiarly Western European sense of time and

hurry. His conclusion at this point is that current attempts to measure inter racial intelligence are premature and all further work on these lines will inevitably be unscientific until further research has been made into the "abilities response mechanisms and manner of thinking and feeling of the Africans. Two examples of such research by Nel and Endeman which he quotes and commends are both unfortunately published in Afrikaans and are therefore virtually inaccessible for consultation by most medical and educational research workers outside the Union.

In examining the effect of home environment on the growth of intelligence the research worker in the Union is placed in a peculiarly difficult position. As Dr Biesheuvel points out African tribal family life develops intelligence in directions almost entirely different from those of the European home. The home environment in tribal society conditions the growing child to become a member of a group where formerly the standards of skills ability and behaviour were laid down by tribal codes and sanctions. In certain remote parts of Africa such tribal society can still be found, but it does not exist anywhere in the Union in an untouched form in spite of the policy of segregation. White

and black society are bound together by economic links which stretch from the towns and industrial centres into the interior of the reserves. Hence in the Union there can be no measurement of intelligence as developed under purely tribal conditions to serve tribal purposes. Dr Biesheuvel decides on other grounds that tribal Africans will have to be excluded from the experimental group for the reason that there can be no parallel European control group with which to compare it. But a very fundamental difficulty then arises. In comparing the home environment of urban Africans with urban Europeans many of the material features of the home may have certain similarities but the general cultural milieu in which the African child is brought up in the cities is neither African nor European. It is a hybrid culture which has not yet been sufficiently studied in any of its aspects sociological economic or psychological so as to provide accurate factual data for measuring home environmental factors. Dr Biesheuvel says emphatically that home environment can only be equated within the same cultural milieu and it is evident to any social research worker that living in the same city does not necessarily produce a similar cultural milieu. Moreover his conclusion after examining such social economic studies of urban African conditions as are available is that the average urban African home environment is bound to stunt very markedly the growth of intelligence of the children reared in it not only by failing to provide those stimuli which alone would enable the most to be made of innate potentialities but also by creating situations which have an adverse effect on such growth as might spontaneously occur.

To all workers in tropical areas the relation of malnutrition to the growth of intelligence will be of great interest. Dr Biesheuvel points out two major difficulties in assessing this particular environmental factor. He considers the clinical method of judging malnutrition as too elaborate for use with large groups and rejects the height weight ratio as being discredited. That leaves us at the present stage without a valid practical method of judging malnutrition. The second difficulty in his view is the inconclusive nature of the evidence that subject to particular conditions the growth and function of the nervous system can be impaired by malnutrition. As a result of reviewing a number of authorities however he comes to the conclusion that qualitative malnutrition if severe permanently impairs intelligence at all age-levels and hence he urges that in measuring intelligence some control should be exercised over the nutritional condition of the experimental group.

The results of diet surveys of Africans in urban areas though so far not correlated with intelligence testing show such a general low level of nutrition that comparisons could only be made with the very lowest income levels among Europeans—that is among the most depressed section of the urban European population. This group as Dr Biesheuvel says would be useless for control purposes in an inter racial study as it would probably represent a genetically inferior sample of the European community.

The result of this analysis is a somewhat negative conclusion. Dr Biesheuvel says categorically that under present circumstances and by means of the usual techniques the difference between the intellectual capacity of Africans and Europeans cannot be scientifically determined. One cannot environmentally equate an African group with a European group without selecting unrepresentative samples.

It is interesting to note that Dr Biesheuvel's doubt about the representative character of samples of the African and European population is in line with a conclusion reached in the United States of America. In 1934 the *Journal of Negro Education* gave a whole number (Vol. III No 3) to a critical summary of the studies on the relative physical and mental abilities of the American Negro. It was recognised that the difficulty of getting fair samples was one



of major importance, and this difficulty was practically insuperable in the southern States, the area where the racial situation shows the nearest parallel to that in the Union. It was stated categorically that "it is impossible to secure fair samplings of Negro and white children of the same age who are equally advanced educationally and have had similar environments."

Must we therefore accept a non possumus? As far as the Union of South Africa is concerned, the dust of the battlefield obscures the main issues. On both sides black and white, emotional attitudes will enter into any attempt to make comparisons of intelligence on inter-racial lines. Too much is at stake in such a study which is directly bound up with the economic and political development of the country. That is no reason however why in other parts of Africa studies should not be made of the various environmental influences and their effect on the growth of intelligence without bringing in the factor of comparison with Europeans. Casual statements are made often about a particular tribe being so intelligent. Dr Baesheuvcl himself refers to such a statement about the Basuto as being intellectually superior to other tribes. As they are outside the Union politically though closely linked with it on economic grounds, they have not been included in any of the surveys reviewed by Dr Baesheuvcl. He asks the question which has constantly puzzled many people in Africa, whether statements about the intellectual superiority of any tribe can be substantiated. He thinks that intelligence tests could be applied to such a problem. Here is an obvious field for a combination of research techniques for the psychologist will need the help of the sociologist and the doctor in the assessment of the home environment and the nutritional factors. It may be unimportant in the scientific field whether certain tribes are proved by such tests to be more intelligent than others. Dr Baesheuvcl thinks that these popular beliefs are unfounded, though until proof is forthcoming no one can make positive statements on the subject. What is however of great importance in the scientific field is the working out of joint research techniques between psychologists, sociologists and doctors. The problems connected with the development of Africa and its peoples particularly in the sphere of education and intellectual advance, cannot be solved by a number of unrelated approaches.

*Margaret Read*

HARPER, F. *Extinct and Vanishing Mammals of the Old World*. pp xv+850  
67 figs. & 1 pl. [Bibliography] 1945. Special Publication No. 12.  
American Committee for International Wild Life Protection New York  
Zoological Park, New York 60 N.Y. [30s.]

The present book is briefly noticed because of the relation of game animals and game extermination to tsetse flies. The volume consists of a relatively brief introduction which explains how the information has been collected and points out the great variety of factors which have caused the disappearance or increasing scarcity of many species of mammal in the Old World. It contains a chronological list showing the approximate dates (generally to a half-century) of disappearance for each continent separately.

The greater part of the book consists of an account of many species arranged under Orders. Some of these species have disappeared or are in grave danger of doing so but some of them as it appears to us are not at the moment greatly reduced or on the danger list.

*P. A. Buxton.*

# TROPICAL DISEASES BULLETIN

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## SUMMARY OF RECENT ABSTRACTS \*

## V LEISHMANIASIS

## GENERAL.

KIRK (p. 180) discusses the evolution of the leishmania infections of man pointing out that although three main types of disease are recognized there is no hard and fast line of demarcation between them. He notes that in the Sudan cases are seen in which the three types merge into or follow one another so that there may be difficulty in differentiating between oriental sore and a primary lesion of kala azar or between muco-cutaneous leishmaniasis and the mucosal lesions of a post kala-azar condition. The reason for these variations is that there exist different strains of the parasites which probably have different virulence and tendencies. The leishmania of kala azar in India the Sudan and the Mediterranean are not identical in all respects—for instance post kala-azar dermal leishmaniasis is common in Bengal but rare in Assam—and there are two well-marked types of oriental sore in Turkestan. KIRK (p. 875) noticed that a monkey which had been inoculated with a strain of leishmania after passage from a human case of kala azar (in the Sudan) through two other monkeys developed lesions resembling those of espundia. Similar lesions occasionally occur in human kala azar in the Sudan and may be due to the characteristics of certain strains of leishmania.

JONES *et al.* (p. 543) describe the successful cultivation of leishmania in the yolk sac of developing chick embryos.

SENEKJIE and LEWIS (p. 977) have devised a slide agglutination test with antigens from cultures of the various leishmania, and serum from rabbits immunized first with killed cultures and later with living cultures. Homologous leishmania are agglutinated to high titre and heterologous to lower titres. It seems that this test may be useful in the diagnosis of human disease.

## VISCERAL LEISHMANIASIS.

SHORTT (p. 100) has written an account of recent research in kala azar with special reference to Assam.

*Epidemiology*

In Tashkent kala azar shows a remarkable focal distribution within the towns in spite of the fact that sandflies are uniformly distributed throughout

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945 v. 42. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

the endemic regions. KHODUKIN (p 356) attributes this to the existence of reservoir hosts, especially dogs and he supports this view by aetiological, clinical and epidemiological evidence, noting particularly that whereas in man the parasites are soon eliminated from the peripheral circulation in dogs they are first present in the extensive multiple papules on the muzzle and later become generalized in the skin. The dog, therefore is held to be the principal reservoir of the disease though there is some evidence of transmission from man to man, and from man to dog. *Leishmania* have not been found in rats, mice or lizards. BATTELLI *et al* (p 977) have found *leishmania* in the spleen and bone marrow of dogs in Eritrea, and FERRO LUZZI (p 100) notes that kala azar is endemic in the lowlands of Eritrea.

SEN GUPTA (p 542) has enquired into the epidemiology of kala azar in Bengal during the period 1931-40 and notes that the distribution of the disease is very unequal. For the whole of Bengal there has been an incidence rate of 210 cases each year per 100 000 of the population—this is so high that the disease still constitutes one of the grave medical problems.

SCOVILL (p 875) has written an account of kala azar in China. The point he particularly makes is that the incidence of the disease has increased considerably as a result of disturbances occasioned by war. Kala azar is common in the north but is almost unknown in the more tranquil south, and the Chinese hold that it follows in the wake of famine, flood and war. CLOW (p 101) describes kala azar in the Province of Shensi, China, where the disease has now become almost epidemic and constitutes a serious problem. Sandflies abound in the months of May and June. It is most common in children and young adults and conforms to the classical type. Treatment consists of administration of various antimonials and of stilbamidine but of 400 patients only 91.5 per cent. were cured or doubtfully cured and 16.3 per cent. relapsed, were moribund or died.

#### *Aetiology Transmission*

SENEKJIE (p 359) after a review of available information concludes that the agent of S. American kala azar which at first was known as *L. chagasi* is identical with *L. donovani*.

ARMYTAGH and BOLLIGER (p 358) have infected a young opossum, while still in the maternal pouch with *L. donovani* by intraperitoneal injection.

MALOVE and BROOKS (p 357) argue that the sandfly transmission of kala azar in India has not been satisfactorily established and quote evidence which, in their opinion is against this method. For details the original abstract should be consulted. In comment WENYON expresses the view that the authors have not refuted the sandfly theory which is receiving increasing support both for kala azar and oriental sore.

#### *Clinical Findings.*

LOWE (p 711) discusses the early diagnosis of kala azar noting the characteristic feature of irregular fever with rapid pulse but without symptoms of toxæmia. The only other early findings are a positive result with the complement fixation test in which the W.K.K. antigen is used [see SEN GUPTA below] and the presence of *leishmania* in sternal puncture material. One condition is essential for early diagnosis namely that the possibility of kala azar should be kept in mind.

BURCHINAL and WOODS (p 635) describe three cases of kala azar in U.S. soldiers who had served in N. Africa and Sicily. In one the only sign was enlargement of lymph glands particularly of the neck. Biopsy confirmed the diagnosis. Treatment with sodium antimony gluconate was given in all these

cases with success stillbamidine was not useful in two of them. ANGEVINE *et al* (p 976) report another case in an American soldier who had served in N Africa or Sicily in which the only sign of kala azar was enlarged lymphatic glands in which the parasites were seen. They describe the histological features of the glands.

If serum from cases of kala azar is kept at 7-11°C for three days a precipitate is formed. WERTHEIMER and STEIN (p 262) show that this is due to a substance allied to euglobulin which they have named the Cold Fraction. This phenomenon persists for long periods after clinical cure and it is not yet known whether in such cases cure can be regarded as complete. The fraction is present in certain other morbid conditions.

SEN GUPTA (p 338) gives an account of the use of the complement fixation test with the Witebsky-Klingenstein and Kohn antigen, for the diagnosis of kala azar. It is usually positive in kala azar and usually negative in other conditions which might be confused with it and is very useful for early diagnosis.

### Treatment

Sodium antimony gluconate (Stibatin Glaxo Laboratories) was used for the treatment of kala azar by BURKE and CHARRAVARTY (p 17) with success in each of 21 cases. It is supplied as a solution of which 1 cc contains 20 mgm. of pentavalent antimony. The daily dose is 1 cc. for each year of age with 15 cc. as the maximum and as much as 100 cc may be given in 7 days by intravenous or intramuscular injection. There were no unpleasant reactions in this series. FERNÁNDEZ CASTAÑYS (p 978) again writes of the successful results obtained in infant kala azar by the use of sodium antimony gluconate suspended in oil and given by the intramuscular route. He thinks that this is the method of choice.

SARROUY and GILLOT (p 101) report favourably on Pentastib (the methyl glucamine salt of para amino-phenyl-stibonic acid) and state that the best results in infant kala azar were obtained when the quantity to be administered was spread over the minimum number of days—viz for each kgm. of body weight 0.07 gm should be injected daily for 4 days or 0.1 gm. daily for 3 days. PATEL (p 263) reports so favourably on Stibatin in kala azar that he regards it as the drug of choice. It has many advantages over neostibosan and urea stibamine. He obtained cure in each of six cases treated.

SEN GUPTA (p 543) reports cases of mixed kala azar and malaria. Antimonials do not affect malaria parasites and quinine does not affect leishmania, but there seems to be a certain antagonism between the infections.

It is known that when stillbamidine solution is kept and especially if it is exposed to light changes occur which render the substance more toxic. Late sequelae of stillbamidine treatment observed by KIRK and HENRY (p 18) were affections of the nervous system (changes in sensation along the course of the trigeminal nerve neuritis of the nerves of the leg rarely epilepsy or mania) or fatal delayed poisoning in coma. These effects did not develop until 1-3 months after the completion of treatment. Stillbamidine is absorbed quickly by the tissues and is released slowly for excretion and as HAWKING points out in comment is in this respect similar to mepacrine. Evidence accumulated that the toxic symptoms were due to chemical changes in the drug which occur when solutions are exposed to light.

FULTON (p 19) has investigated the therapeutic action of certain newer aromatic diamidines on *L. donovani* infections of hamsters. For details the original should be consulted. FULLER (p 264) writes of a colour reaction for aromatic diamidines previously described by DEVINE to which he has made certain modifications. Details are given in the original abstract.

FULTON (p. 978) found that penicillin had no action in experimental infection of hamsters with the leishmania of Indian kala azar.

GOODWIN (p. 262) in a critical examination, has shown that examination of smears from the cut surface of the spleen of animals infected with *L. donovani* and counting parasites against cell nuclei, is a reliable method of estimating the progress of the disease and the effect of treatment. It is necessary however to count up to 1 000 cell nuclei if the numbers of leishmania are small in order to obtain a reliable result. The organisms are fairly evenly distributed through an infected spleen.

### CUTANEOUS LEISHMANIASIS ORIENTAL SORE

#### General Treatment

FAROOQ and QUTUBUDDIN (p. 978) have found oriental sore in as many as 42-68 per 1 000 of the population in part of Hyderabad State the majority of cases were in children under 10.

ELKERTON (p. 543) notes that most of the cases of oriental sore in an Indian Military Hospital were in members of a cavalry unit, or in men engaged in transport and therefore associated with horses. He thinks, therefore, that *Stomoxys calcitrans* may be implicated in transmission. Treatment of these sores by scraping under general anaesthesia, and subsequent dressing with tannic acid powder was successful, but the injection of atabrin was tried and was found to have certain advantages.

KOJEVNIKOVA (p. 454) has found that the moist type of oriental sore tends to occur on the limbs and the dry type on the face. The same author (p. 876) describes cases in which oriental sore developed at the site of existing trauma of the skin, and hazards the opinion that sandflies are attracted to such areas in preference to intact skin.

BERBERIAN (p. 877) has shown experimentally that dogs can be infected with *L. tropica* with the development of cutaneous lesions, but not of visceral lesions. The skin lesions of dogs in nature, which are sometimes attributed only to kala azar may in fact be due to oriental sore.

BAKHRAMI (p. 454) describes the technique of cultivating *L. tropica* in the chick embryo.

BALL and RYAN (p. 19) quote their experience which shows that Neostam (Burroughs Wellcome & Co.) is very effective in the treatment of oriental sore. Intravenous injections are given twice each week, and increase from 0.05 to 0.2 gm each to an average total of about 1.14 gm. Toxic reactions may be reduced by giving the injections at noon and withholding the midday meal, or they may be controlled by morphine. In 231 American soldiers thus treated, there were no failures. The average time for cure was 14.5 weeks. Neostam seems to be the most effective means of treatment of oriental sore.

KLITNER (p. 455) describes the technique of cultivating *L. tropica* in the chick embryo.

GUPTA and KAHALI (p. 191) have made a pharmacological study of umbellal time, which is derived from *Berberis* and is allied to berberine. It apparently has a useful action in the infiltration treatment of oriental sore.

#### Immunity

BERBERIAN (p. 102) states that the immunity eventually produced by an oriental sore which heals is complete, but he has shown by experiments in man that it takes a long time to develop about 240 days after inoculation of infective material. During this period, therefore, sores additional to the

deliberately produced sore may be acquired. Immunity does not develop until the papule ulcerates and commences to heal and the leishmania disappear naturally from the lesion. He (p. 359) has previously found that the incubation period after injection of cultures of *L. tropica* was 2 weeks to 6 months but he now quotes three cases in which this was as long as 18 to 56 months.

The same author (p. 360) has shown that suspensions of cultivated *L. tropica* in isotonic saline will remain viable for 17 days at temperatures varying from 15.8° to 38.3°C. This observation was made to meet the need of physicians who require suspensions for purposes of immunization.

BERBERIAN (p. 360) has attempted to confirm previous work by PESSÔA and PESTANA, who claimed that inoculation of *L. tropica* killed by phenol would produce immunity to oriental sore. His results were entirely negative and no immunity to infection was found in two persons so inoculated though immunity was proved in others who had recovered from sores produced by the injection of living flagellates.

KATZENELLENBOGEN (p. 361) has followed up the results of vaccination in 416 people near the Dead Sea in Palestine where oriental sore is hyperendemic. The incubation period varies from about 2 weeks to 18 months. In 45 persons a febrile reaction occurred probably allergic in nature but in only four of these did a vaccination sore develop. In 27 others no vaccination sore followed though they had no evidence of previous oriental sore the possibility of natural immunity is to be considered. The vaccination campaign has produced very favourable results of 25 persons newly arrived in the district and vaccinated none has had a natural sore in a period of 2 years whereas of 70 not vaccinated 65 have had sores in the same period.

#### MUCO-CUTANEOUS LEISHMANIASIS (AMERICAN)

KEAN (p. 359) states that an endemic focus of cutaneous leishmaniasis has been found in Arraiján, Panama, and describes the clinical features of the disease. A striking feature in several cases seen in the Gorgas Hospital during the present century has been nodular lymphangitis in areas draining the ulcers. Treatment with antimony potassium tartrate or Fouadin is successful. STEWART and PILCHER (p. 712) report a case which they claim to be American muco-cutaneous leishmaniasis, in a boy who had never left Texas.

COSTA (p. 544) describes American leishmaniasis in which the lesions may be mistaken for those of yaws.

LOPES and LAENDER (p. 979) have found that the Montenegro skin test is the method of choice for the diagnosis of mucocutaneous leishmaniasis in the clinics and health centres of the interior of Brazil.

BELTRÁN (p. 361) has found it impossible by reducing the pH of culture media below 7.2 to eliminate bacteria from cultures of *L. brasiliensis* without killing the leishmania.

PIFANO (p. 191) gives a list of sandflies which may be vectors of *L. brasiliensis* in one region of Venezuela.

PESSÔA and VILLELA (p. 712) report favourably on the results of treatment of American muco-cutaneous leishmaniasis with the German preparation Antimon-ditoxin which appears to be more useful than tartar emetic and Fouadin. SNOW (p. 544) had no success in the treatment of a case of American cutaneous leishmaniasis with penicillin.

Charles W. Silcock

## MALARIA

AUSTRALIAN MILITARY FORCES Malaria in the Borneo Operations May 1-  
 Sept. 1 1945 [ENGLISH J C. Lt. Colonel Malariologist Adv H.Q  
 AMF] RFA (46) 4 16 mimeographed pp [Med. 5/1]

— Destruction of Adult Mosquitoes in the Early Stages of an Operation  
 [MACCALLUM W P Brigadier DDGMS Adv L H Q] Technical  
 Circular No 4 1945 June 6 4 mimeographed pp [Med. 45/195/172.]

The incidence of malaria was low in Tarakan. After the landing very few anophelines were found. *A. kochi* was most in evidence. Only two *A. leucos* *phyrus* breeding places were found and only one adult *A. umbrosus* was captured. The island is small its population was static and mostly congregated near the controlled areas of the oil wells and the port. None of 325 children examined had an enlarged spleen and only two of 220 children harboured malaria parasites, *P. vivax* in each case. Among 600 adults the only positive blood films obtained during a 2 week period were *P. vivax* 21 *P. falciparum* 9 and *P. malariae* 1 all the parasite carriers were Indonesian labourers imported from the mainland by the Japanese.

In Labuan Island before the war mosquito control measures had been limited to an area of 2 square miles in the town of Victoria. The common mosquitoes were *A. kochi*, *A. barbirostris*, *A. hyrcanus*, *A. sundensis*, *A. leucos* *phyrus*, *A. tessellatus*, *A. kawaii*, *A. separatus*, *A. umbrosus* and *A. philippinensis*. After the arrival of the Japanese mosquito control practically ceased the tide gates were broken and *A. sundensis* breeding became common in the town area. Detailed information is lacking regarding the incidence of malaria before the war but *P. falciparum* malaria was said to be rare and cerebral malaria almost unknown. The Japanese imported heavily infected Javanese labour and used people who had previously lived in a controlled area for clearing and cultivation. Malaria became rife. At the time of the allied landings the spleen rate in Malay children was 75 per cent. During the first 3 weeks of July some 100 of the 8000 local natives were treated for malaria amongst whom there were eight cases of cerebral malaria and one of blackwater fever.

In Brunei town malaria had been severe prior to 1935. An antimalaria organization was established in that year and by 1939 the spleen rate in 561 children in the river kampong had been reduced to 1 per cent. On the arrival of the Japanese the inhabitants of the river kampong fled to the hills and rice-growing districts some 60 per cent of them contracted malaria there. They drifted back malaria control in the town was discontinued and the incidence of malaria increased. The Japanese also suffered severely some of them dying from cerebral malaria. *A. kochi* was the commonest mosquito in the town. *A. leucos* *phyrus* and *A. barbirostris* were common in the outskirts.

In Kuala Beluar Seria there was considerable malaria in 1932. The land was covered with swamp forest with a narrow sandy coastal strip. The vector was *A. umbrosus*. *A. sundensis* was not common. As clearing proceeded the latter species replaced the former as the chief vector. Antimalarial work increased in efficiency and there was but little malaria from 1939 to 1941. Other species of mosquito found in this area were *A. kochi*, *A. tessellatus*, *A. separatus*, *A. maculatus*, *A. kawaii*, *A. leucos* *phyrus* and *A. basalis*. All organized antimalarial work ceased after the Japanese occupation in December 1941. There was an increase of *A. umbrosus* and later of *A. sundensis* breeding. Native labour was recruited from highly malarious inland villages. In 1944 the malaria rate was higher than it had ever been, even before control work.

Most of British North Borneo was highly malarious blackwater fever was not uncommon among Chinese and Malays Dr MACARTHUR found *A. leucosphyrus* to be the chief vector in N W Borneo it breeds in thick jungle *A. maculatus* is considered to be unimportant *A. umbrosus* and *A. hyrcanus* are said to have been incriminated in certain parts In Weston spleen rates of 55 and 54 were found in Malay and Chinese children respectively

But little information was available about pre war malaria in Balikpapan the town was well controlled but the surrounding districts were malarious After the occupation anophelines taken included *A. sundaticus* *A. leucosphyrus* *A. leucosphyrus hackeri* *A. hyrcanus nigerrimus* *A. tessellatus* *A. kochi* *A. vagus* *A. separatus* *A. kunteri* *A. bazzas* *A. barbirostris* *A. notum* *A. brosius* *A. albolaciniatus* and *A. montanus* (?) *A. sundaticus* *A. leucosphyrus* and *A. hyrcanus nigerrimus* are regarded as vectors in East Borneo others are *A. maculatus* *A. umbrosus* *A. minimus* (on Lacet Island) and *A. hyrcanus sinensis* A survey of 333 children under 5 years of age soon after the landing revealed a spleen rate of 43 per cent A parasite survey of 277 natives employed as carriers showed *P. vivax* 17 and *P. falciparum* 24

The incidence of malaria among the troops was low mepacrine suppression was good. It is not possible to summarize all the control measures employed but new developments call for note Of great interest is the information given concerning the destruction of adult mosquitoes by drifting mists Two types of mist were used pyrethrum spray from aerosol dispensers Freon bombs and DDT 24-5 per cent in kerosene or distillate The Freon bombs were mostly used indoors in intact or partly destroyed houses tunnels closed pill boxes etc but their outside use was also tried The dosage varied from 4 to 12 seconds spraying per 1 000 cubic feet The measure was effective especially against *Aedes* mosquitoes The outside use of Freon bombs was advanced against *Aedes* mosquitoes in areas of jungle and scrub where *Aedes* were prevalent The method adopted was that of walking along bush tracks at the rate of a yard a second with a discharging dispenser in either hand or of placing them on the ground at 15-yard intervals and allowing them to discharge for 60 seconds at each location

Five per cent DDT mist was used only out of doors The most satisfactory equipment was an American 3-gallon decontaminator pressure sprayer with a Rega nozzle of 0.08 in aperture. As a means of control against dengue fever this method appeared to be of the greatest use. The camp area in which a case of dengue occurred including an area of 100 to 200 yards around it was thus sprayed

The use of DDT applied to walls tents mosquito nets etc. for residual effect proved its value.

For larval control in service conditions the use of plaster of paris and saw dust pellets soaked in 5 per cent DDT in oil was very convenient and effective Two parts of sawdust and one part of plaster of paris by volume are mixed with water and allowed to set The mixture is then cut into pellets of from half to one cubic inch and allowed to dry (48 hours) The pellets are then soaked in 5 per cent DDT in oil for a further 48 hours and are then ready for use. Their effectiveness was 100 per cent. for 2-4 weeks in suitable breeding places They may be thrown a considerable distance to breeding places difficult of access and are ideal for collections of water in bomb craters tanks drums etc. while their use in ricefields is harmless.

The use of suppressive mepacrine prevented malaria incidence being used as an index of the efficiency of mosquito control in the Borneo operations. The very low incidence of dengue however among susceptible troops landed in areas where dengue is endemic is strong evidence of the efficiency of that control. During the first 10 weeks of the operations there were 44 cases of



[June 1948]

dengue in Tarakan, 208 in Brunai Labuan and 85 in Balikpapan. At the end of 10 weeks very few cases were occurring in any area. The lowest incidence of dengue occurred in the area where most use was made from the earliest days of ground spraying with DDT mists, particularly in camps in which dengue had occurred.

The incidence of malaria was surprisingly low. Up to the end of September only 114 cases of *P. falciparum* malaria had occurred, 55 in Balikpapan, 35 in W. Borneo, 4 in Morotai and 0 in Tarakan, among forces totalling 57 000 during an average period of 12 weeks.

Norman White

PAL, R. On the Bionomics of *Anopheles culicifacies* GÜm. Part II. The Ecology of the Immature Stages. *J. Valaria Inst of India*. 1945 June, v 6 No. 1 53-74 1 fig & 1 chart 24 refs)

Part I of this paper was concerned with the longevity of *Anopheles culicifacies* (this Bulletin 1944 v 41 448). In the second part the author discusses the results of his laboratory experiments on the aquatic stages of the mosquito and compares them with observations made in the field. It is known that *A. culicifacies* breeds in irrigation channels, pools in river beds, borrow pits and cement tanks and that it can adapt itself to almost any type of water. Experiments showed that there was no consistent preference for any particular type of water. Ovipositing females avoided soapy water, polluted stagnant and distilled. The author concludes that eggs are scattered at random, and that this accounts for the presence of *A. culicifacies* larvae in all kinds of breeding places.

Experiments to discover the time of oviposition showed that 60.1 per cent. of eggs were deposited between 19.00 and 22.00 hours, 27.6 per cent. were laid between 22.00 and 01.00 hours and 12 per cent. between 01.00 and 04.00 hours. Thus, eggs laying continued throughout the hours of darkness but most were laid during the first third of the night. The number obtained in these tests varied very little from season to season. The number obtained in these tests is given as 115 to 134.

In the laboratory, ovipositing females showed slight preference for cooler water when given a choice between 38°C. (102.4°F) and 42°C. (107.6°F) between 38°C. and 45°C. (113°F) however the warmer water was definitely avoided. Eggs larvae and pupae exposed to constant temperatures between 28°C. (82.4°F) and 37°C. (98.6°F) with the optimum development was between 28°C. (82.4°F) and 32°C. (89.6°F) for eggs 45.5°C. at 32°C.

Thermal death points were found to be 53°C. (127.4°F) for eggs 45.5°C. (113.9°F) for fourth stage larvae and 43.3°C. (109.9°F) for pupae. In small natural breeding places the maximum surface temperature during the hot summer months was rarely as high as 44.8°C. (112.8°F) but 43°C. (109.4°F) was common. In large ponds it rarely rose above 37°C. (98.6°F). In May and June therefore *A. culicifacies* deserts the hot pools and channels and resorts to the cooler wells and tanks. In December and February the maximum water temperature ranged between 10°C. (50.0°F) and 15°C. (59.0°F). At such temperatures the life-cycle takes about three months. In the laboratory eggs were killed at temperatures below 10°C. and most larvae and pupae died when kept at 5°C. or below.

Results obtained from a long series of experiments to investigate the effects of free and saline ammonia on oviposition and on development of larvae showed

that female *A. culicifacies* laid eggs indiscriminately in concentrations as high as 120 parts per million but that larvae ceased to develop in concentrations exceeding 12 parts per million. This may partly account for the absence of this anopheline from highly ammoniacal waters.

The effect of organic pollution of breeding places was studied by preparing specially polluted water in the laboratory, withdrawing samples at intervals for analysis and allowing gravid females the choice of ovipositing in the withdrawn samples. The females and the immature stages were seen to be fairly sensitive to organic pollution. If it exceeded 1064.50 parts per million females were repelled and larval development ceased.

From several experiments designed to investigate the effect of light and shade on oviposition the author's conclusion is that shade itself had no appreciable influence but females were sometimes unable to lay eggs because of the mechanical obstruction caused by the object producing the shade.

Figures relating to the experiments are set out in 13 tables in the text and in five appendices.

Malariaologists and entomologists will find this paper a useful contribution to our knowledge of the bionomics of an important mosquito.

H S Leeson

RAO T R. Behaviour of *Anopheles fluviatilis* Part III. Larvae Habitats in North Kanara District. *J Malaria Inst of India* 1945 June v 6 No 1 77-82.

Nocturnal movements and day time resting habits of *Anopheles fluviatilis* were dealt with in Parts I and II of this series of papers [this *Bulletin* 1944 v 41 641 1945 v 42 625]. This third paper discusses 9,526 collections of *Anopheles* larvae made in the North Kanara district by the Bombay Provincial Malaria Organization between August 1942 and December 1944.

With the object of obtaining more precise information regarding the breeding places of *A. fluviatilis* the collection figures were analysed and are presented in two tables.

Altogether 2,557 larvae of *A. fluviatilis* were collected and of this number 1,678 (65.6 per cent.) were from streams and channels. There were 3,616 searches in streams and channels and 493 (13.6 per cent.) yielded *A. fluviatilis* larvae. Out of 797 searches in fallow rice fields, 42 (5.3 per cent.) and out of 1,386 in growing rice fields 102 (7.4 per cent.) yielded *A. fluviatilis* larvae. The species was more prevalent in rice fields in 1944 than in the earlier period. Out of 157 searches in swamps 40 (25.5 per cent.) produced larvae of this species though this type of breeding place was relatively uncommon, small and easily dealt with it should not be ignored. The *kutcha* field wells situated in rice field valleys were also found to be breeding *A. fluviatilis*.

Thus while it is confirmed that streams and channels are the generally preferred breeding places of this anopheline the author suggests that intensive studies may reveal that *A. fluviatilis* breeds in rice fields swamps and wells more commonly than has been believed and that these places may in some localities be more important even than streams and channels.

H S Leeson

ZOLOTOREV E K. [*Anopheles maculipennis* of Northern Iran.] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 2 50-57 1 map [In Russian.]

This paper deals with the distribution and ecology of *Anopheles maculipennis* in Iran. The identification of subspecies was based on the eggs laid by captured females 5,000 of which produced 1,000 batches of eggs.

was found that along the Iranian coast of the Caspian Sea, *A. maculipennis* is represented by three subspecies: *typicus subalpinus* and *sacharovi*. *A. m. maculipennis* occurs at the foot of the northern slopes of Elburz and on the eastern slopes of Bagrov Dag and Talish, as well as along a narrow strip of low lands on the west and east coast. *A. m. subalpinus* is also characteristic for the maritime plains of Sefidrud and Babol while *A. m. sacharovi* inhabits the steppe zone of the eastern Caspian lowlands and is not found to the west of the town Babolser. As regards the ecological requirements of the different subspecies of *A. maculipennis*, *A. m. maculipennis* is associated with waters originating in the mountains occurring both at high altitudes and in basins of rivers fed from mountain sources. *A. m. subalpinus* is found in standing waters of the humid maritime lowlands and in rice fields while *A. m. sacharovi* occurs only in waters of high salinity in the sand steppes. C. A. Hoare

HEILIG R. Malaria in Diaguha. *Indian Physician* 1945 Nov v 4 No 11 237-43

This address deals with many pathological conditions that malaria infections may simulate and some interesting illustrative cases are recorded. The combination of malaria with pneumonia is serious but sulphonamides and quinine or atabrin can be used simultaneously without giving rise to any untoward effects. A case is recorded which suggests that pleurisy with effusion may be caused by malaria. A patient in whom the symptoms had suggested a diagnosis of coronary thrombosis was found to have a heavy *P. falciparum* infection and was cured with quinine. Malaria may closely simulate amoebic hepatitis, and malaria attacks occasionally present all the features of gall-stone colic. The case history of a patient in whom malaria seems to have caused a pylorospasm of allergic origin is of interest. Malarial dysentery, malarial nephritis and malarial ascites are discussed. Cerebral malaria may begin, and end fatally without any rise of temperature. Persistent hiccup may occur in acute as well as in chronic malaria and only yields to antimalarial treatment. The address ends with the warning that even the heaviest malarial infection does not exclude the possibility of a co-existing appendicitis, puerperal sepsis or urinary tract infection. Norman White

THONNARD-NEUMANN E. Zur Pathogenese der Malaria Anämie. (The Pathogenesis of Malarial Anaemia.) *Deut. Tropenmed. Ztschr.* 1944 Apr-May v 48 Nos 7/10 129-47 4 figs.

The author studied the blood and bone marrow in 34 cases of malaria of which 26 were *P. vivax* infections, 7 *P. malariae* and 1 *P. falciparum*. Five cases were natural infections, the rest were induced, all but three by means of blood injections. The patients were allowed 10 paroxysms and then treated with quinine, atabrin or a new preparation. The clinical picture varied widely: the *P. falciparum* case was fatal.

Daily blood parasite and reticulocyte counts were made. Red blood cell counts and haemoglobin estimations were made twice weekly. In the therapeutic cases, sternal bone marrow was examined four or five times during and subsequent to the malarial attack; the bone marrow was examined once only during the attack in the natural infections.

At the commencement of the infection the mean red blood cell count was 4.5 million per cmm. and the mean haemoglobin value 80 per cent. At the end of the infection the mean red count had fallen to 2.7 million and the mean haemoglobin to 60 per cent. The colour index was estimated in 22 cases of *P. vivax* infection. It was equal to or less than 1 in 15 out of 22 cases on the

first day greater than 1 in 19 out of 22 at the end of the malarial attack and equal to or less than one subsequent to treatment. The mean red cell diameter reached a maximum at the height of the infection in the 10 cases of *P. vivax* infection examined (7.65 $\mu$  compared with 7.3 $\mu$  on the first day and 7.35 $\mu$  after treatment)

Before infection the reticulocytes in 20 cases varied between 1 and 14 per thousand red cells. During the malarial attack the reticulocytes did not increase in the peripheral blood except in one case in which they reached 25 per thousand red cells. Five days after the commencement of treatment however there was a reticulocyte crisis which in one case reached 175 reticulocytes per thousand red cells. One-third of the cases showed a reticulocyte count of more than 60 per thousand red cells after treatment. Some cases showed a double wave of reticulocytes after treatment a depression in numbers developing with the temporary reappearance of plasmodia in the peripheral blood.

During the malarial attack the bone marrow showed erythropoietic activity with a big increase in reticulocytes which were about eight times as plentiful as in the peripheral blood (the normal ratio of reticulocytes in bone marrow and peripheral blood is given as 3:1). Megaloblasts were seen in two cases only, one of which was the fatal malignant tertian infection.

After cure there was a rapid increase of reticulocytes in the peripheral blood and a corresponding rise in the bone marrow reticulocytes.

In the *P. vivax* cases the infection rate of the reticulocytes in the bone marrow was the same as that in the peripheral blood. The stages of plasmodial development seen in the marrow were the same in proportion as those in the peripheral blood except that gametocytes were more common in the latter. There was no evidence of increased damage to the reticulocytes in the bone marrow and the number of plasmodia found in the bone marrow was not greatly in excess of that found in the peripheral blood.

The author considers that the fact that there was no increase in reticulocytes in the peripheral blood during the acute malarial attacks although during this period the reticulocytes increased in the bone marrow indicates that the plasmodia must interfere in some way with the discharge of reticulocytes from the marrow into the peripheral circulation. After disappearance of plasmodia from the blood stream this inhibition ceases.

Anaemia in benign tertian and quartan infections therefore developed mainly from the destruction of red cells by the plasmodia, and was associated with an inhibition of the discharge of young red cells from the marrow.

B G Macgregath

NOE W L, JR GREENE C C, JR & CHENEY G. The Natural Course of Chronic Southwest Pacific Malaria. *Amer J Med Sci* 1946 Feb 1; 211 No 2: 215-19. 2 charts.

The object of this study was to observe the natural course of relapsing *P. vivax* malaria, acquired in the Southwest Pacific, when uninfluenced by specific treatment. It was hoped to ascertain whether or not immunity might develop with sufficient rapidity to justify withholding specific therapy. Seventy-two patients volunteered. 25 of these received no specific treatment of any sort at the Hammond General Hospital where the observations were made. Nineteen received specific treatment at some time during the observations for administrative reasons only. Seventeen had to receive specific treatment for all clinical activity because of the severity of their infections. Two had parasitaemia only. These patients had previously had from 1 to 16 relapses which had been treated the average number being 8.64 for 69 patients. They were under observation for 2 to 10 months.

June, 1946

These patients were thus mostly in the chronic relapsing stage of the infection in which frequent recurrences have become well established—Phase 2 as the authors term it. When specific therapy is withheld Phase 2 is characterized by relapses each of which may include recurrent bouts of chills and fever which tend to assume the single tertian pattern. Each relapse may last from 1 day to more than 3 months. The average duration of 113 untreated attacks was 5-47 days. Between febrile bouts (month temperature 100°F or over) there may be malaise, headache and generalized pains. Parasites are found in the blood during the active periods of this phase. Clinical activity may subside after a single bout of fever or may recur for months. During the final stage of the infection (Phase 3) parasitaemia is constantly or irregularly present but the temperature does not rise above 100°F. An occasional late relapse might occur though none was noted in this series. Phase 3 lasted for 10 to 80 days in 30 cases which were completely followed. It apparently represents the development of immunity and perhaps cure. Phase 2 ordinarily lasts many months and Phase 3 many weeks. No specific therapy is therefore not justified.

The commonly observed cyclic recurrences at regular intervals in chronic South West Pacific malar infections treated with atabrine (mepacrine) are rare if treatment be withheld.

Norman White

ANDREW R. A Syndrome in Vivax Malaria probably due to Spontaneous Subcapsular Haemorrhage of the Spleen. *Med. J. Australia* 1945 Dec 22, 2 No 25 400-64

Among 6038 patients suffering from *P. vivax* malaria ten developed symptoms strongly suggestive of subcapsular haemorrhage of the spleen. In all the onset of the syndrome was marked by the sudden occurrence of very acute pain in the left upper quadrant of the abdomen. In four cases pain was severe in the left upper quadrant and in six, pain was referred to the tip of the acromioclavicular process of the left shoulder. There was no trauma. Six patients were lying in bed when pain seized them. One was awakened by pain. Two were sitting down and one was in the act of swallowing beer. The pain was accentuated by deep breathing and lasted from a few days to many weeks. In three cases there was tenderness in the left hypochondrium but no true rigidity. A small pleural effusion, signs of pulmonary congestion and complicating pneumococcal pneumonia were all observed. None of the patients was submitted to operation and all recovered.

All the patients had acquired the malaria infection in New Guinea. The syndrome occurred in three cases early in the 6 weeks maintenance course of during treatment. In two cases three months after an attack of malaria. Five patients had a history of previous malaria. Five had none. There was no fever apart from that caused by still active malaria. The pulse rate was not raised except in the first hour or two of very severe pain. The leucocyte counts were normal.

Only one of three conditions appears at all likely to have been the cause of this syndrome—a small rupture of the spleen, a splenic infarct, or a subcapsular haemorrhage of the spleen. In splenic rupture acute abdominal pain of sudden onset such as characterized these cases, is not common. Moreover it is unlikely that 10 consecutive cases of rupture of the spleen should have recovered without operative treatment. The blood findings in two patients did not suggest that a haemorrhage of any great size had occurred. The diagnosis of splenic infarct is more difficult to exclude. The shoulder pain, and the symptoms

and signs in the pleural sac and the base of the left lung are unlikely however to have been caused by an infarct. Infarcts in the spleen may occur in malaria without causing signs or symptoms. A sudden stretching of the splenic capsule as the result of haemorrhage is the most likely explanation of the sudden abdominal pain and tenderness. The consequent irritation of the diaphragm would explain the shoulder pain and the restriction of normal diaphragmatic movement would account for the changes at the base of the left lung.

LOWE J. Malaria contracted after Splenectomy for Splenomegaly probably caused by Kala-Azar. *Indian Med Gaz* 1945 Nov. 80 No 11 568

Splenectomy was performed on a male patient who was admitted to a Calcutta hospital in 1944 with an enlarged spleen the condition being diagnosed as tropical or Bengal splenomegaly. he recovered uneventfully and was discharged in March 1945. A month later he was readmitted with fever which was diagnosed on clinical grounds as due to kala azar and thus diagnosis was supported by the positive result of a complement fixation test made with WKA antigen and by the response to treatment for kala azar.

In July 1945 he had another attack of fever which lasted for 2 weeks before he came to the School of Tropical Medicine where his blood showed *Plasmodium vivax*. He was admitted to hospital with a temperature of 104.8°F and his liver was enlarged down to the level of the umbilicus. Treatment with mepracrine was effective and he was discharged from hospital a week after admission. The author thinks that the enlargement of his spleen was caused by kala azar which was not diagnosed, that the long duration of malarial fever before treatment was owing to the absence of his spleen and that the great enlargement of his liver during the malarial attack was compensatory for the absence of the spleen. The case indicates that diagnoses of kala azar and malaria should be excluded before splenectomy is done and that persons whose spleens have been removed should treat malaria with more than ordinary respect.

HOWE C. D & DUFF F. L. Effect of Altitude Anoxia in provoking Relapse in Malaria. *Science* 1946 Feb 22 223

In summary neither relapse nor parasitemia was observed in a group of 50 individuals giving histories of recent malaria within a period of 7 days following exposure to the anoxia produced by a 1 hour stay at 18 000 ft. in a low pressure chamber.

LIPPINCOTT S. W. ELLERBROOK L. D. HESSELBROCK W. B. GORDON H. H. GOTTLIEB I. & MARBLE A. Liver Function Tests in Chronic Relapsing Vivax Malaria. *J Clin Investigation* 1945 Sept. 24 No 5 616-22

1 fig [19 refs]

Liver function tests were carried out in a group of 317 patients during and subsequent to attacks of relapsing *P. vivax* malaria treated in most cases by atabrine. The tests used were bromsulphthalein retention after 45 minutes cephalin flocculation galactose tolerance intravenous hippuric acid synthesis determination of icterus index and serum bilirubin serum albumin globulin cholesterol and phosphatase and urinary urobilinogen estimations. Bromsulphthalein was retained 45 minutes after injection in 4 per cent of 49 cases in whom the test was made on the second and third day of the malarial attack. Two to forty four weeks after the attack 3 per cent of 149 patients still showed bromsulphthalein retention.

Cephalin flocculation tests were carried out for the first five consecutive days of the acute attack in 42 patients. The results depended to some extent upon the antigens used (Difco and Wilson) but some abnormal flocculation was found.

Galactose tolerance was normal in 4 to 52 weeks after the attack. Hippuric acid synthesis was tested in 56 men following recurrent malarial attacks, and in 28 normal subjects. The malarial subjects showed some slight depression of synthesis. Icterus index and serum bilirubin were increased slightly during the first days of the malarial attack, but were normal after the attack. Urobilinogen was found in the urine at a dilution of more than 1 in 20 during the early days of the attack but by the fifth day the concentration was within normal limits. The blood proteins were estimated in 172 patients 1 to 28 weeks after an attack in all the albumin content was normal and in three the globulin was raised above 2.7 gm per 100 cc. Only two patients had lowered total protein.

The authors conclude that there is some evidence of transient disturbance of liver function during recurrent attacks. There is little indication of permanent damage.

B G Macgregor

MARIO S. On Three Cases of Idiosyncratic Urticaria in Course of Relapsing Malaria. *Indian Med Gaz.* 1945 Nov v 80 No 11 567

PARVIZ M. Observations de paludisme héréditaire et congénital. Paludisme du nourisson. Congénital Malaria. *Rev Paludisme et Méd Trop* 1946 Feb 15 4 No 23 33-8

ROGAN J M & COOMES A E R. Some Aspects of Malaria Therapy on the Eastern Frontier of India 1942-44. *Indian Med Gaz.* 1945 Nov v 80 No 11 572-81

In 1942 the authors were deputed to investigate the efficacy of the standard army treatment of malaria among troops in the field in Assam. This standard treatment comprised quinine 30 grains daily for 2 days, mepacrine 0.3 gm daily for 5 days a rest period of 2 days then pamaquin 0.02 gm daily (0.03 gm for British troops) for 5 days.

In an Indian General Hospital in a village in a highly malarious jungle four methods of treatment were compared: the standard method as above; and pamaquin standard treatment modified by continuing the quinine treatment till fever had subsided; standard treatment modified by commencing mepacrine and pamaquin administration. Ninety-two cases were treated by each of these methods each group containing 43 (19 32 *falciparum* and 17 mixed infections). The results showed that the standard treatment was effective for the treatment of the acute stage of uncomplicated cases of malaria occurring under war conditions in Assam. There was no evidence that the malaria encountered in Assam was resistant to treatment. There was no appreciable difference between the response of Indian and British troops to treatment. There was no difference between the results obtained with the synthetic drugs of Bayer's and of British origin respectively. The early relapse rates were moderately high repeated reinfections were probably taking place.

In another series of observations in an Indian General Hospital in Gauhati, Assam five methods of treatment were compared: (1) the army standard treatment (2) mepacrine 0.2 gm. every 6 hours for 48 hours then 0.1 gm. thrice daily for 5 days (3) mepacrine 0.2 gm. thrice daily for one day then

0.1 gm thrice daily for 6 days (4) the same treatment as the last followed by pamaquin 0.01 gm. thrice daily for 3 days alkali was given during the mepacrine course to render the urine alkaline before pamaquin was taken (5) initial single dose of 0.8 gm. mepacrine followed by 0.1 gm. thrice daily for 7 days Two hundred patients were treated by each method they were all Indians After treatment the patients were sent to a convalescent depot in Shillong which is malaria free for a month's observation

The results showed that all five methods were about equally effective in controlling fever and parasitaemia in the control of fever quinine was slightly more effective than mepacrine in vivax infections but less so in *falciparum* infections Irrespective of the treatment used it took ten days and thirty days from the day of admission for the erythrocytes in vivax malaria to regenerate to the level found on admission and to five million red cells per cmm respectively Corresponding periods for *falciparum* malaria were 25 days and 40 days [Shillong is 4500 ft above sea level blood-counts of healthy residents are likely to be much higher than five million] No abnormality in total or differential leucocyte counts could be attributed to any of the treatments used. Vomiting was the most common sign of intolerance this was least common with moderate doses of mepacrine (treatments 3 and 4) and most common in patients treated with an initial dose of 0.8 gm mepacrine (treatment 5) The standard treatment was the least effective in preventing relapse during the observation period. With the treatments employing mepacrine only the relapse rate was inversely proportional to the total dosage of mepacrine Pamaquin after a light mepacrine treatment appeared to reduce the relapse rate

As a result of these observations the following recommendations were made that quinine and pamaquin be omitted from the routine treatment which should consist of mepacrine only commencing with a moderately high dosage and that this be followed by suppressive mepacrine treatment

BURNHAM R. C. Acute Atabrine Intoxication Report of a Case. *U.S. Navy Med Bull* 1946 Mar v 46 No 3 434-8. Norman White

A case is described in which acute intoxication by a single dose of more than 90 grains of atabrine resulted in complete recovery without apparent liver damage The patient's suicidal motivation is discussed from the psychiatric viewpoint as representative of a considerable group of suicides.

FITZBUGH O G NELSON A. A. & CALVERY H O with the technical assistance of J M GLASSMAN The Chronic Toxicity of Quinacrine (Atabrine). *J Pharm & Exper Therap* 1945 Nov v 85 No 3 207-21 1 fig & 1 chart. [17 refs.]

Previous experiments by WRIGHT and LILLIE [this *Bulletin* 1944 v 41 99] and by SIEGEL and MUSHETT (*ibid* 1945 v 42 178) showed that quinacrine (atabrine mepacrine) could cause pathological lesions in animals when given in large amounts It was earlier established that the drug accumulates in the tissues. SCUDI and HAMLIN [this *Bulletin* 1944 v 41 728] reported that rats fed on a high protein low fat diet were best able to counteract the toxic effects of the drug When the diet was adequate HEGSTED *et al* [this *Bulletin* 1944 v 41 849] showed that the addition of certain vitamins gave no increased protection The present authors have demonstrated differences in the toxic effects produced by giving quinacrine by mouth to albino rats for practically



For therapeutic purposes the standard course of Paludrine in *P. falciparum* infection was 300 mgm. daily for 10 days. With this treatment, radical cure of 12 out of 12 trophozoite-induced and of 64 out of 65 sporozoite-induced, infections resulted. Smaller dosages readily brought about rapid disappearance of trophozoites but the clinical response to treatment was not so rapid. The dosage used in *P. vivax* infection varied from a single dose of 100 mgm. to 1.0 gm. daily for 14 days. The clinical response to treatment was not rapid, and showed little variation with the different dosage schedules. Parasites soon became degenerate but remained in the blood during 5-8 days of therapy the result being dependent to some extent on the amount of drug given and on the original density of parasites. With the maximum dosage of the drug relapses occurred in sporozoite-induced infections after freedom from malaria for 29-88 days but they had not been noted after a considerable period in a few cases treated for overt trophozoite-induced malaria with small doses of drug. The results of treating overt mixed infections were similar to those for the single infections. Of 41 soldiers treated with the standard course of drug for overt *P. falciparum* infection acquired in New Guinea, 12 developed *P. vivax* infections 19-33 days after the last dose of Paludrine but malignant tertian parasites were absent. In two cases of quartan malaria the clinical response was rapid, but parasites disappeared only slowly. It will be seen therefore that Paludrine proved efficient in the clinical cure of the three forms of malaria but that the response was not more rapid than with quinine or mepacrine. The radical cure obtained in *falciparum* infections was according to the authors "in accord with the concept that there are no persistent e.e. forms in *falciparum* malaria, and that radical cure will result from therapy with an efficient schizonticide. It appeared that the number of secondary attacks occurring after treatment of sporozoite-induced *P. vivax* infections with Paludrine was smaller than would have been expected had other known antimalarials been used.

Gametocyte production in *P. falciparum* infections appeared to be unchecked by the standard course of Paludrine. The appearance of these sexual forms in the blood remained unchanged during therapy for a period normally observed when treatment with other non-gametocidal drugs is given. The salivary glands of mosquitoes did not, however become infected and a considerable amount of experimental evidence was obtained regarding the infectivity of gametocytes for mosquitoes after therapy ended. Blood containing gametocytes was then non-infective for mosquitoes for 4-12 days, depending on the dosage which had been given. The drug appeared to exercise its effect on the growth of the parasite in the insect and maturation of the oöcyts present was prevented. The gametocytes of *P. vivax* were unaffected in number or morphology by Paludrine. Either development of oöcyts in the mosquito was prevented or chitinization occurred in those partly developed.

Regarding the mode of action of Paludrine it appeared from a study of the blood parasites in *P. falciparum* infections that the drug affected either the amoeboid forms or a later stage in the schizogonous cycle. This view was confirmed by *in vitro* experiments. It was noted that division of chromatin was arrested, and the asexual cycle thus brought to an end. In studying the action on the (postulated) e.e. forms of this parasite 30 volunteers were given various doses of Paludrine at different times relative to the bites of infected mosquitoes. Some were fully protected, and from others undergoing treatment blood was subinoculated to fresh hosts on the 7th day after exposure with negative results, while those in controls were positive. The evidence available to date indicated that Paludrine in certain doses was a true causal prophylactic and that its action was not on the sporozoite but on a later stage in the cycle of development. These results—considered with others obtained

earlier in which not all cases of overt malaria from sporozoite-induced infections were cured by certain doses of the drug—lead the authors to believe that the e.e. forms are more susceptible to its action than erythrocytic forms. There is other evidence to support this view. Paludrine also has a powerful action on the maturing schizonts of *P. vivax*. In view of the fact that it was in general unable to effect radical cure of this infection produced by mosquitoes indicated that some action took place on sporozoites or e.e. forms whereby the development of the primary wave of parasites was inhibited. In this respect the drug acts as a causal prophylactic but not all e.e. forms are destroyed. In certain circumstances it is believed to act as a complete causal prophylactic.

The toxic symptoms which occurred during therapy were few and not of a serious nature. They were associated generally with maximum dosage of 1.0 gm daily and included vomiting diarrhoea and abdominal pain. Red cells epithelial cells and hyaline casts have been noted in the urine while in one case there was gross haematuria. These symptoms were readily relieved by withholding or reducing the dose of drug which has a wide range of effective action or by clinical cure of the disease. In other cases there was an increase in the myelocytes of the peripheral blood some days after the treatment began possibly as a result of the drug's action on the bone marrow. J. D. Fulton.

MEDICAL J AUSTRALIA 1946 Feb 16 v 1 No 7 234-6 Researches on "Paludrine" (M 4383) in Australia. From the Land Headquarters Medical Research Unit Cairns FAIRLEY N H (Director)] This is an account of the researches recorded in the paper abstracted above in addition a short history of the preceding chemotherapeutic investigations is given.

KNOWLES F L. & FISK F W DDT Water Emulsion in Rice Fields as a Method of controlling Larvae of *Anopheles quadrimaculatus* and other Mosquitoes. *Pub Health Rep* Wash. 1945 Aug 31 v 60 No 35 1005-19 11 figs (2 on 1 pl.)

Flooded rice fields are often habitats for the larvae of anopheline mosquitoes but because of their extent and the susceptibility of growing rice to injury ordinary larvicidal methods are apt to be limited and expensive. The authors have endeavoured to find a safer effective and cheaper method of controlling the breeding of *Anopheles quadrimaculatus* in rice fields by applying a DDT emulsion to the flooding water at the pumping station which supplies the water.

The experiments took place in the Stuttgart area of Arkansas U.S.A. where the flooding water is pumped from deep wells or reservoirs and carried to the fields in canals. The experimental fields were of two sizes six plots of 12-18 acres each and 30 plots of 1/20th of an acre each. Different kinds of rice were sown in different plots but the method of culture was the same in all.

To determine the prevalence of mosquito larvae a sampling routine was established both in the treated and in the untreated fields. In the six large plots the sampling stations were at varying distances from the water entrance. In the small plots two sampling stations were located one at each end. Fifteen negative dips were regarded as sufficient 20 dips were taken if larvae were scarce and never less than ten if larvae were numerous. After a few days sampling was done weekly. Larvae of the rice field mosquitoes (*Psorophora ferox* and *P. discolor*) were common at the beginning of the season and

also after the first flooding but later larvae of *Anopheles quadrimaculatus* were most abundant. Larvae of *Culex erraticus* were also present.

The larvicide consisted of DDT (1 part) a solvent (3 parts) and Triton X 100 (1 part). The solvents were xylol, Culicide B oil, Dendrol or xylol plus Culicide B oil. A description is given (and a diagram) of the apparatus for dispensing the larvicide on the large plots at the rate of 0.1 p.p.m. in the flooding waters at the pump. The delivery rate was checked and recorded every half hour at the outlet. To the small plots DDT was applied individually in concentrations ranging from 100 to 0.1 p.p.m.

Data obtained from 23 000 larval counts are discussed and analysed in nine tables, comparing DDT dosage, solvent, type of plot, distance from water inlet and the counts made in untreated ricefields. The larval counts in the large plots, irrespective of the treatment or the dosages, increased with the distance from the water inlet, thus indicating a loss of toxicity as the water flowed through the canals. Generally speaking treated fields contained 50 per cent. fewer *Anopheles quadrimaculatus* larvae and 72 per cent. fewer culicine larvae than untreated fields, although the fish *Gambusia* was present in the untreated but not in the treated fields. In the small plots, both anophelines and culicines were completely controlled by DDT concentrations of 1.0 p.p.m. and 0.2 p.p.m., respectively. There was no residual toxicity after one application.

The authors conclude that the addition of DDT to the flooding waters as it enters the ricefields will reduce the breeding of mosquitoes but will not eradicate them. It is considered that the rice suffered no injury from the DDT treatments; indeed, there was an increase in the rice yield, perhaps as a result of the toxic effect of DDT on the rice water weevil [*Lissorhoptrus oryzae*] though this may not be the sole reason.

H S Lesson.

JONES H. A. DEONTER, C. C. BURWELL, R. W. & KNIPPLING E. F. Larvicidal Aerosols containing DDT. *J. Econom. Entom.* 1945 Aug. v. 38 No. 4 432-3.

A mist or aerosol of DDT prepared by the emission of a DDT in methyl chloride solution from an aerosol cylinder is lethal to anopheline larvae up to a distance of 60 ft. from the place of emission. Tests were carried out in a very large room in which pans of water were exposed to varying aerosol doses of DDT. Larvae of *Anopheles quadrimaculatus* subsequently placed in pans exposed at 20, 30, 40 and 60 ft. were killed, and it was shown by the subsequent addition of five larvae that the pans at 20 and 30 ft. distance received a sufficient dose of DDT to remain toxic to larvae despite repeated artificial rain, for a period of 27 days.

Field tests confirmed that the method could be of practical value and full control was achieved with a dosage of 0.1 lb. per acre on swamps of up to 750 sq. ft.

G Macdonald

WISECUP C. B., BURWELL, R. W. & DEONTER, C. C. DDT Sprays Mechanically Dispersed for Control of Anopheline Mosquito Larvae. *J. Econom. Entom.* 1945 Aug. v. 38, No. 4 434-6.

A difficulty in the use of DDT as an anopheline larvicide is that the required dose of oil solutions is so small that their regular and even distribution presents technical difficulties. Aerosol bombs have been shown to be a convenient means of distribution, and in the work recorded in this paper the authors tried distribution in the aerosol form with hand atomizers, power sprayers, a large chemical sprayer of the Flit-gun type, knapsack sprayers and the "decontamination type of spray cylinder". The last two were the most efficient for

the treatment of large rather inaccessible breeding areas they are presumably pneumatic sprayers from which the fluid is ejected by direct air pressure on its surface and is mechanically scattered by a nozzle stated to be of 56 to 60 gauge orifice and a whirl plate

By this means it proved possible to treat very large areas. For instance in one breeding place 287 100 sq ft in extent full control was achieved up to 500 ft. from the point of application but the results depended very greatly on the wind—variable gusty or strong winds interfered with the even deposition of DDT. In consequence the method is reliable only in the hands of well-trained and observant operators. The authors conclude that distribution in must form should be of especial value where potholes hoof prints wheel ruts and other small depressions provide scattered breeding places or in breeding areas that are difficult to treat because of depth of water.

[As an anopheline larvicide DDT will not be used to its full value until means of distribution are devised which take full advantage of the minute doses needed. Both distribution in mists and distribution by discrete application of small doses from an oil-can as described by RIBBANDS (this *Bulletin* 1946 v 43 409) appear to have definite advantages over more conventional methods and each will probably have its own sphere of utility. The reviewer hopes that other workers will specify more exactly the type of apparatus used as colloquial descriptions and trade names are not generally comprehensible.]

G Macdonald

ANDERSON B G The Toxicity of DDT to *Daphnia*. *Science* 1945 Nov 23 539

This is a note to the effect that DDT in concentrations of 1 to 100 parts per billion [thousand million] of water immobilizes *Daphnia magna*. Less than 1 part per billion is ineffective. These results may be important in relation to the use of DDT for mosquito control since in many localities it is essential that the zooplankton be protected.

Charles Wilcocks

DEONIER C C & JONES H A TDE, 1,1-Dichloro-2,2-bis (p-Chlorophenyl) Ethane, as an Anopheline Larvicide. *Science* 1946 Jan. 4 13-14

The compound TDE (which differs from DDT in having only two chlorine atoms on the ethane nucleus instead of three) was tested for toxicity to larvae of *Anopheles quadrimaculatus*. The tests were made by comparing TDE and DDT in (i) acetone suspensions (ii) impregnated talc dusts and (iii) fuel-oil solutions which were atomized and allowed to settle on the water containing the larvae.

In all tests the TDE appeared to be very slightly more toxic than DDT (except that the "knock-down" with a 0.01 p.p.m. acetone suspension was rather quicker with DDT than with TDE).

J R Busvine

## BLACKWATER FEVER.

YULE C L, GOLD M A & HINDS E. G Hemoglobin Precipitation in Renal Tubules. A Study of its Causes and Effects. *J Exper Med* 1945 Nov 1 v 82, No 5 361-74 3 text figs & 4 figs on 1 pl. [22 refs.]

The authors review the literature on the question of the genesis of the syndrome of renal failure associated with intravascular haemolysis. They point out that such syndromes all have in common the circulating pigment

a factor " of vascular or chemical nature affecting the organism as a whole and a specific kidney lesion with varying degrees of tubular degeneration and obstruction of tubules by pigmented casts in the convoluted and collecting tubules and ascending loops of Henle.

The theories concerning the cause of the kidney changes in the syndrome are briefly discussed.

The authors investigated the problem by injecting solutions of haemoglobin into rabbits which were secreting acid or alkaline urine and in which the kidney tubules were damaged either by temporary clamping of the renal artery [see SCARFF and KEELE *Bulletin of War Medicine* 1944 v 4 370] or by the previous poisoning of a specific poison in this case sodium tartrate.

White domestic rabbits were used and given a diet of rabbit chow and vegetables (for the production of alkaline urine) or oats and stale bread (for the production of acid urine). Water was allowed freely with both diets. The haemoglobin solution was obtained from citrated rabbit's blood. The doses of haemoglobin injected were the equivalents of the amount set free by the lysis of the cells in 200 to 400 cc. human blood. Selective tubular damage was obtained by clamping the renal artery (in previously unilaterally nephrectomized animals) for 15 or 25 minutes or by the subcutaneous injection of 20 per cent. sodium tartrate in doses of 0.8 to 0.95 gm. per kilo.

Preliminary experiments showed that the injection of the haemoglobin solution into normal animals was not followed by evidence of renal dysfunction whether the urine was acid (two animals) or alkaline (two animals).

Following the clamping of the renal pedicle for 15 minutes (the haemoglobin solution was injected 5 minutes before the release of the pedicle) haemoglobin casts were found in the animals with acid urine but were "not so numerous" in the animals with alkaline urine. In two animals with acid urine there was a pronounced rise of blood urea N after the injection of haemoglobin one animal developed temporary oliguria.

When the renal artery was clamped for 25 minutes there was a transitory rise in blood non-protein nitrogen (N.P.N.) which returned to normal in 7 days with short periods of oliguria and anuria. In the animals with alkaline urine the rise of blood N.P.N. was more persistent and there was transient oliguria. In two animals with acid urine there was a sharp rise in N.P.N. following haemoglobin injection, and both became anuric. Both died on the fifth day and there were haemoglobin casts in the tubules in both. A third animal with acid urine showed a rise in N.P.N. without accompanying change in urine volume. This animal was killed on the eighth day and was found to have many haemoglobin casts in the tubules the renal pedicle had been clamped a month previously and there was some scarring of the pedicle. The authors suggest that the result obtained may have been due to failure to occlude lateral circulation through the scar tissue.

In the tartrate experiments the degree of renal damage was maximal in the animals secreting acid urine. Haemoglobin casts appeared in both groups of animals after injection of haemoglobin they were more numerous in the animals passing acid urine. Blood N.P.N. rose moderately after tartrate injection in both "acid" and "alkaline" animals. There were only minor changes in urinary volume. In the animals injected with haemoglobin subsequent to injection of tartrate a rise of N.P.N. (above that already produced by the tartrate injection) occurred in one (of 4) "alkaline" animals and two (of 4) "acid" animals. Urinary volume was unchanged in one "alkaline" animal, is not stated in another and was reduced in two one animal going into intermittent anuria. The alkaline animal showing a rise of N.P.N. died on the fifteenth day there were no tubular casts but there was a high degree of tubular necrosis and some calcification. Urinary volume was reduced in

two of the acid animals and in two it is not stated. One animal died in oliguria the other was killed on the twelfth day, there were many haemoglobin casts in the former and occasional casts in the latter.

The authors conclude from their experimental results that the precipitation of haemoglobin in the renal tubules is not primarily dependent on the reaction of the urine but on functional abnormality of individual nephrons indicated histologically by lesions of the tubules. These alterations in the tubules are non-specific since they can be produced by either ischaemia or chemical poisoning (tartrate).

Given the combination of renal tubular damage and haemoglobinuria urinary pH may be important since pigmented (haemoglobin) casts are more common in animals secreting acid urine than in those secreting alkaline urine.

B G Macgregor

BUTTS D. C. A. The Rh Factor in Blackwater Fever. A Preliminary Note  
*Amer J Trop Med* 1945 Sept v 25 No 5 417-20 [30 refs.]

In this preliminary note the author suggests that a factor concerned in the development of blackwater fever may be isoimmunization to an Rh like substance present in malarial plasmodia. According to WIENER (quoted as a personal communication) isoimmunization to the Rh factor occurs in 2-4 per cent. of Rh negative individuals following transfusion with Rh positive blood or the birth of an Rh-positive foetus. From this the author calculates the possible incidence of blackwater fever per 1 000 using LEVINE's figures for the incidence of the Rh factor in whites, negroes and Chinese. He compares his calculated results with figures recorded by various authors for the incidence of blackwater fever and erythroblastosis foetalis in whites and negroes. The following table (from the text) summarizes findings —

	Ratios	
	White	Negroes
(a) Cases of blackwater fever (calculated)	30 to 60	9 to 18
(b) Cases of blackwater fever (Deeks and James, 1911)	33 to 59	2.5 to 5.9
(c) Deaths from erythroblastosis foetalis	37	2

The figures in the table are misleading. The ratios in line a of the table are based on figures giving the incidence of blackwater fever per 10 000 cases of malaria; those in line b are based on figures giving the incidence of blackwater fever per 10 000 of the racial population. The two sets of figures are therefore not comparable. The author may be excused this error on the grounds of the incredible obscurity of both text and tables in the report by Deeks and James (DEEKS W. E. and JAMES D. M. *Report on Haemoglobinuric Fever in the Canal Zone* I.C.C. Press 1911 32) but his figures in line c of the table can be due only to bad arithmetic: the real proportion calculated on the basis of deaths from erythroblastosis foetalis per 10 000 foetal deaths is nearer 3 to 1 than his figures of 37 to 2 [see POTTER *Bulletin of Hygiene* 1941 v 16 59]. The rest of the paper deals shortly with aspects of multiple cases of blackwater fever in the same family, stillbirths and blackwater fever and the rôle of antimalarial drugs in blackwater fever.

B G Macgregor

PETERS J T Origin and Development of a New Therapy for Crush Injury Transfusion Kidney and a certain Number of other Diseases. *Acta Med Scandinavica* 1945 v 123 No 1 90-100 5 figs.

The author states that after an autopsy on a woman who had died of mercuric chloride poisoning he decided to search for "a satisfactory explanation as to how the tubular epithelial cells with almost undamaged glomeruli could produce anuria. Just the reverse would have been expected with such a destruction of the elements of reabsorption." An artificial nephron was constructed and experiments with this suggested that increased intrarenal pressure was an important factor in producing oliguria and anuria.

The author lists 32 diseases including blackwater fever in which oliguria or anuria accompanied by uraemic symptoms may occur. He advises decapsulation of the kidneys as an emergency operation in such conditions.

[The paper is diffuse and unconvincing. The author quotes from a letter from the Editor of the *Lancet* stating that "The treatments which you recommend—decapsulation, diuretics and pressor drugs—are now widely used, separately or in combination." B G Macgregor.]

### TRYPANOSOMIASIS.

RIDLEY H. Ocular Lesions in Trypanosomiasis. *Ann Trop Med & Parasit* 1945 Oct. 10 v 39 No 2, 66-82. [51 refs.]

During the years 1943-44 ophthalmic examinations were performed by the author on 215 West African patients suffering from trypanosomiasis. These patients comprised 39 African soldiers, 44 African civilians (a high proportion of whom were selected on account of past or present eye complaints and whose attendance for ophthalmic examination was arranged) and 132 other African civilians entirely unselected, who happened at the time to be attending trypanosomiasis dispensaries. Of these 215 patients 64 were found to have ophthalmic complaints and 32 of these had lesions of the retina and visual pathway caused by the toxic effects of therapeutic arsenic. Of the remaining 32 who had inflammatory changes in the structure of the eyes in 10 they were attributable to onchocerciasis in 14 to miscellaneous injuries and infections and in only 8 they were regarded as directly due to trypanosomiasis. These eight comprised one patient with nystagmus parkinsonism, with severe mental derangement, two who showed bilateral papilloedema of moderate degree which was observed to subside during treatment, four in whom the indefinite disk edges and the presence of new connective tissue in the physiological cups and around the central retinal vessels suggested that a similar condition had at one time been present, and only one in whom otherwise unexplained keratitis was found. The keratitis was interstitial and whether or not it was directly due to trypanosomiasis remains in doubt, for it was not possible to examine the eye microscopically for the parasite. The cases with swollen optic disks are confidently reported as papilloedema and not as papillitis because there was little or no visual impairment even in the acute stage and because no degree of pallor followed resolution of the swelling. It is possible that the secondary optic atrophy and narrowed retinal vessels reported by observers who had the opportunity of examining the fundus oculi in a large number of untreated patients may in some instances have resulted from chronic papilloedema. Other cases may be due to onchocerciasis.

The supreme importance of onchocerciasis as a cause of ocular inflammations including keratitis iridocyclitis choroidoretinitis and optic atrophy in trypanosomiasis patients is demonstrated by this investigation and the author has been able when visiting trypanosomiasis clinics in the Gold Coast to find unsuspected cases of ocular onchocerciasis and to confirm the diagnosis by the demonstration of intraocular microfilariae. Onchocerciasis is without doubt the predominant cause of ocular inflammations in trypanosomiasis subjects.

The miscellaneous lesions require little comment being such as might occur in any series of inhabitants of the African bush.

The following conclusions are drawn from the author's observations —

1 In man inflammations due to the presence of trypanosomes within the tissues of the eye are rare and as yet no case has been proved by microscopical examination. The substantia propria of the cornea is the part most likely to be affected.

2 Such inflammations are practically confined to the terminal stages of the disease shortly preceding death. Intraocular trypanosome infection cannot be regarded as a common or important cause of impaired sight in Africa.

3 Ocular abnormalities are found in uncomplicated trypanosomiasis but these are secondary to infection of the meninges and central nervous system and resemble those found in other forms of lymphocytic meningo-encephalitis. The commonest of these is papilloedema which may develop in the acute stage of infections of only moderate severity. More rarely ophthalmoplegias, Argyll Robertson pupils and nystagmus occur.

4 Concurrent onchocerciasis is common and ophthalmologically important. This disease in all probability accounts for the majority of cases of intraocular infections, keratitis, iridocyclitis, choroidoretinitis and very possibly optic atrophy when occurring in untreated cases previously attributed to trypanosomiasis.

5 The risk of amblyopia and even amaurosis from therapeutic arsenic is serious.

E O G KIRMAN

NELSON J W The Treatment of Rhodesian Trypanosomiasis with Penicillin.  
*East African Med J* 1945 Dec v 22 No 12, 407-8

The patient was a man in an advanced stage of Rhodesian sleeping sickness unlikely to live for more than a few weeks if no treatment were given while treatment with the usual drugs would have been useless. penicillin was therefore tried.

He was in a stuporose state unable to answer questions and incontinent. the superficial lymph glands were not enlarged. very slight oedema of the legs was present. Trypanosomes were numerous in the blood and cerebrospinal fluid and the latter showed 0.1 per cent. of protein and 566 cells per cmm. 96 per cent being lymphocytes. Other blood findings were erythrocytes 5 360 000, haemoglobin 12.6 gm (90 per cent Sahli), formal gel +10 minutes opacity ++, serum proteins 8.8 gm — albumin 3.4 gm, globulin 5.4 gm. Kahn reaction negative. E.S.R. 97 mm in 1 hour 117 mm in 2 hours.

He was treated with penicillin as follows: 20 000 units i.m. every 3 hours for 7 days; 40 000 units i.v. on the first day; 20 000 units intrathecally on the 2nd and 6th days; total, 1 250 000 units in 8 days.

Trypanosomes were found in the cerebrospinal fluid on the 2nd day [of treatment ?] but not on the 6th day nor after death which occurred on the 16th day after admission. they were present in the blood throughout. After death the cerebrospinal fluid contained 0.5 to 1 unit of penicillin per cc.



LOWE J. Kala Azar [Correspondence.] *Trans Roy Soc. Trop Med & Hyg* 1946 Feb v 39 No 4 345-6.

In a recent paper by SHOKIT [this *Bulletin* 1946 v 43 317] Lowe is quoted as saying that urea-stibamine is as effective as any of the new preparations the author explains that this drug is cheap fairly safe and effective and is therefore suitable for the treatment of outpatients in India, but has the disadvantage that it must be given intravenously. Some other preparations may be slightly more effective e.g. neostibosan which is not cheap and has not been available for some years diamidino-stilbene which is unsuitable because it produces toxic reactions and "solustibosan" (sodium antimony gluconate) the value of which, however cannot yet be estimated. "Aminostiburea" is apparently identical with urea-stibamine and is even cheaper while stibatin (Glaxo) appears to be the same as solustibosan.

The author prefers sternal puncture to splenic puncture and reserves the latter for old-standing cases in which sternal puncture has given negative results. J F Corson

HALAWANY A. & JALILI M. Investigation into the Effect of Penicillin on *Leishmania Tropica* *J Roy Egyptian Med Ass.* 1945 Aug v 28 No 8, 394-6.

"1. Sodium penicillin in a concentration of 1000 units does not possess any effect on leptomastix forms of *Leishmania tropica* in culture.

2. The application of dressings soaked in an aqueous solution of sodium penicillin possessing a strength of 20 Oxford units to each c.c. of distilled water or normal saline cures the secondary infection but has no effect on the lesion itself. The same can be said of the application of ointment containing 200 units of sodium penicillin in each gram of vaseline.

## FEVERS OF THE TYPHUS GROUP

FITZPATRICK Florence K. Studies on Cultivation of Rickettsiae in Eggs. *J Lab & Clin Med* 1946, Jan., v 31 No. 1 45-55 [37 refs.]

This paper contains a number of useful technical hints in connexion with the cultivation of rickettsiae in yolk sacs. It should be read by all who are engaged in this work. Only a few examples are given in this summary.

The rickettsial strains employed were the Breinl epidemic, the "Wilmington murine," and two of "spotted fever" (Rocky Mountain spotted fever).

Eggs from pullorum tested flocks of white Leghorn hens were used. In most cases they were inoculated at the 7-day incubation period. Smears were stained by a modification of the Macchiavelli method in which the basic fuchsin was diluted with sterile distilled water which had not been neutralized. Methylene blue was used in staining smears for testing sterility. The fragments of yolk sac used for making smears were taken from the point of attachment to the embryo.

Chick embryos of the 8th or 9th days were found most suitable for inoculation with "spotted fever" rickettsiae. Incubation at 34-35°C. gave the best results with all strains.

With epidemic and spotted fever strains chick embryos were more susceptible than guinea-pigs to minimum doses of infection. With endemic strains little difference in susceptibility was observed. Contrary to what happens with viruses the addition of immune serum to the rickettsial inoculum did not delay the death of the chick embryos.

No antigen was detected in the yolk substance so long as the embryos were still alive but several hours after death the yolk contained soluble antigen, derived, presumably from autolysis of the yolk sacs. For experimental study of the antigens it was found better to omit either treatment of the suspensions and to add 1.0 per cent. formalin instead of 0.1 per cent. the stronger formalin apparently delays the disintegration of the rickettsiae

ZARAFONETIS C J Serologic Studies in Typhus-Vaccinated Individuals. I. The Effect of a Stimulating Dose of Typhus Vaccine on the Weil-Felix and Complement-fixing Antibodies. *J Immunology* 1945 Nov v 51 No 5 365-74 [11 refs.]

John W D Morgan

The author working with the U.S.A. Typhus Commission in Cairo studied the Weil-Felix and complement fixation responses in 100 persons who had previously received standard courses of Cox type epidemic typhus vaccine and in nearly every case two to five later stimulating doses of the vaccine at three monthly intervals. In every case the last of the stimulating doses had been given at least three months before the first test was carried out. All the sera were tested and immediately a further stimulating dose was given to each person. Later tests were made at intervals of two and eight weeks.

The Weil-Felix titre (OX19) was 1-40 to 1-80 in 17 cases just before the stimulating dose two weeks later these titres were reached in 21 cases so that the changes in the reaction were insignificant. The reaction with OX2 was negative in every case and only one person gave a positive reaction (1-160) with OXK the titre being the same before and after the stimulating dose. No explanation could be found for this reaction.

In the complement fixation tests both epidemic and murine antigens were used. Before the final stimulating injection 21 persons were positive with epidemic antigen and seven of these were also positive with murine antigen. Two weeks after the injection 70 persons were positive with epidemic antigen and 34 of these were also positive with murine antigen but usually at considerably lower titres. The findings in 27 cases are shown in a table from which the following analysis has been prepared by the reviewer —

Complement Fixation Reactions

Titres observed	Epidemic Antigen			Murine Antigen		
	Before injection	After 2 weeks	After 8 weeks	Before injection	After 2 weeks	After* 8 weeks
Negative	18	0	13	24	8	17
1-4 to 1-8	7	4	9	3	15	9
1-16 to 1-32	2	19	5	0	4	0
1-64 to 1-128	0	4	0	0	0	0

\*In one case no test was made

From the original table it appears that two weeks after the injection seven persons had titres half as high (1-4 to 1-16) as their epidemic titres (1-8 to 1-32) and eight weeks after the injection two who gave negative epidemic reactions were positive (1-4) with murine antigen. One other gave the same titre with both antigens and two had a murine titre half as high as the epidemic titre.

LOWE J. Kala-Azar [Correspondence.] *Trans Roy Soc Trop Med & Hyg* 1946 Feb. v 39 No 4 345-6.

In a recent paper by SHORTT [this *Bulletin* 1946 v 43 317] Lowe is quoted as saying that urea-stibamine "is as effective as any of the new preparations the author explains that this drug is cheap fairly safe and effective and is therefore suitable for the treatment of outpatients in India, but has the disadvantage that it must be given intravenously. Some other preparations may be slightly more effective e.g. neostibosan, which is not cheap and has not been available for some years diamidino-stilbene which is unsuitable because it produces toxic reactions and solustibosan" (sodium antimony gluconate) the value of which however cannot yet be estimated. Aminostibarea "is apparently identical with urea-stibamine and is even cheaper while stibatin" (Glaao) appears to be the same as solustibosan.

The author prefers sternal puncture to splenic puncture and reserves the latter for old-standing cases in which sternal puncture has given negative results  
J F Corson

HALAWANY A. & JALILI M. Investigation into the Effect of Penicillin on *Leishmania Tropica*. *J Roy Egyptian Med Ass.* 1945 Aug v 28 No 8 394-6

"1 Sodium penicillin in a concentration of 1000 units does not possess any effect on leptomastix forms of *Leishmania tropica* in culture.

2. The application of dressings soaked in an aqueous solution of sodium penicillin possessing a strength of 20 Oxford units to each c.c. of distilled water or normal saline cures the secondary infection but has no effect on the lesion itself. The same can be said of the application of ointment containing 200 units of sodium penicillin in each gram of vaseline."

## FEVERS OF THE TYPHUS GROUP

FITZPATRICK Florence K. Studies on Cultivation of Rickettsiae in Eggs. *J Lab & Clin Med* 1946 Jan., v 31 No 1 45-55. [37 refs]

This paper contains a number of useful technical hints in connexion with the cultivation of rickettsiae in yolk sacs. It should be read by all who are engaged in this work. Only a few examples are given in this summary.

The rickettsial strains employed were the "Breuil epidemic, the Wilming-ton murine and two of spotted fever" [Rocky Mountain spotted fever].

Eggs from pullorum tested flocks of white Leghorn hens were used. In most cases they were inoculated at the 7-day incubation period. Smears were stained by a modification of the Macchiavello method in which the basic fuchsin was diluted with sterile distilled water which had not been neutralized. Methylene blue was used in staining smears for testing sterility. The fragments of yolk sac used for making smears were taken from the point of attachment to the embryo.

Chick embryos of the 8th or 9th days were found most suitable for inoculation with spotted fever rickettsiae. Incubation at 34-35°C. gave the best results with all strains.

With epidemic and "spotted fever" strains chick embryos were more susceptible than guinea-pigs to minimum doses of infection. With endemic strains little difference in susceptibility was observed. Contrary to what happens with viruses the addition of immune serum to the rickettsial inoculum did not delay the death of the chick embryo.

No antigen was detected in the yolk substance so long as the embryos were still alive but several hours after death the yolk contained soluble antigen derived presumably from autolysis of the yolk sacs. For experimental study of the antigens it was found better to omit either treatment of the suspensions and to add 1.0 per cent formalin instead of 0.1 per cent. the stronger formalin apparently delays the disintegration of the rickettsiae

John W. D. McGraw

ZARAFONETIS C. J. Serologic Studies in Typhus-Vaccinated Individuals. I. The Effect of a Stimulating Dose of Typhus Vaccine on the Weil-Felix and Complement-fixing Antibodies. *J. Immunology* 1945 Nov 51 No 5 365-74 [11 refs.]

The author working with the U.S.A. Typhus Commission in Cairo studied the Weil-Felix and complement fixation responses in 100 persons who had previously received standard courses of Cox type epidemic typhus vaccine and in nearly every case two to five later stimulating doses of the vaccine at three-monthly intervals. In every case the last of the stimulating doses had been given at least three months before the first test was carried out. All the sera were tested and immediately a further stimulating dose was given to each person. Later tests were made at intervals of two and eight weeks. The Weil-Felix titre (O<sub>1</sub>19) was 1-40 to 1-80 in 17 cases just before the stimulating dose two weeks later these titres were reached in 21 cases so that the changes in the reaction were insignificant. The reaction with OX<sub>2</sub> was negative in every case and only one person gave a positive reaction (1-160) with OXA the titre being the same before and after the stimulating dose. no explanation could be found for this reaction.

In the complement fixation tests both epidemic and murine antigens were used. Before the final stimulating injection 21 persons were positive with epidemic antigen and seven of these were also positive with murine antigen. Two weeks after the injection 70 persons were positive with epidemic antigen and 34 of these were also positive with murine antigen but usually at considerably lower titres. The findings in 27 cases are shown in a table from which the following analysis has been prepared by the reviewer —

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From the original table it appears that two weeks after the injection seven persons had titres half as high (1-4 to 1-16) as their epidemic titres (1-8 to 1-32) and eight weeks after the injection two who gave negative epidemic reactions were positive (1-4) with murine antigen one other gave the same titre with both antigens and two had a murine titre half as high as the epidemic titre

The complement fixation titres showed a pronounced tendency to return to the pre-injection level within eight weeks of the stimulating dose and the degree of cross-fixation with purified murine antigen "was greater than anticipated"

[The cross-fixation referred to is of interest in connexion with the problem of the relationship between epidemic and murine rickettsiae. Anomalous responses in "endemic-typhus" patients who had previously been inoculated with epidemic vaccine have also been reported by PLOTZ and WERTMAN this *Bulletin* 1946 v 43 429] and the degree of cross-fixation observed by the author was much greater than that found by BERTSON [below] for different strains of *Rickettsia orientalis* its occurrence may be regarded as favouring the view that *R. prowazeki* and *R. mooseri* are variants of the same species of rickettsiae rather than distinct species.

Further investigations will doubtless throw light on these and other puzzling findings obtained in the complement-fixation test as applied to the fevers of the typhus group]

John W D Meager

ZARAFONETIS C J Serologic Studies in Typhus-Vaccinated Individuals. II. The Effect of Non-Typhus Fevers on the Weil-Felix and Complement-fixing Antibodies. *J Immunology* 1945 Dec. v 51 No. 6 375-88.

In this paper the author provides a reply to the important question — Are typhus-vaccinated persons likely to give rising titre reactions with the Weil-Felix and complement-fixation tests in attacks of fevers other than typhus? For all practical purposes the answer is—no!

The present study deals with tests of sera from 104 vaccinated persons suffering from such febrile illnesses as nasopharyngeal catarrh, lobar pneumonia, febricula, atypical pneumonia and malaria. The amount of vaccine received prior to the illness ranged from three to eight ml. Among the patients 12 gave positive Weil-Felix reactions at titres ranging from 1-40 to 1-160 with *Proteus* OX19 and two reacted at 1-40 to 1-80 with *Py* OX2. The titres in every case remained constant throughout the illness and no positive reactions appeared among patients who were initially negative.

The complement-fixation reaction with epidemic typhus antigen was positive 1-4 to 1-256 in 55 of the patients—the usual titres were 1-4 to 1-16. Those who gave positive reactions were tested also with murine antigen and 29 reacted at titres of 1-4 to 1-128. Usually the epidemic titre was twice to four times as high as the murine but in seven cases the same low titre of 1-4 was observed with both antigens. This relatively slight difference between the epidemic and murine titres corresponded with the results observed by the author in his earlier study of the reaction in vaccinated persons [see abstract above].

The titre rose during the febrile attack in eight cases but in seven of these the rise was either from 0 to 1-4 or a doubling of the earliest observed titre and in the one case in which the rise was from 0 to 1-8 the patient had received a booster dose of vaccine two days before the onset of the fever. There was therefore no evidence of the occurrence of rises in the titre such as occur in attacks of typhus fever.

The high proportion of positive complement fixation reactions observed in this group is largely explained by the considerable number of the persons who had received booster doses of vaccine within the previous two months.

The author points out that with the complement fixation test a titre as low as 1-4 can be accepted as indicating a positive reaction because no instances of non-specific reactions in properly controlled tests have been reported up to the present time.

John W D Meager

RUBIN S S An Allergic Reaction following Typhus-Fever Vaccine and Yellow-Fever Vaccine due to Egg Yolk Sensitivity *J Allergy* 1946 Jan. v 17 No 1 21-3

MOOSER H & LÖFFLER, W Ein Fall sogenannter Brill'scher Krankheit in Zurich. Ein Beitrag zur Hypothese der späten Rückfälle beim klassischen Fleckfieber [A Case of the So-Called Brill's Disease in Zurich.] *Schweiz med Woch* 1946 Feb 23 v 76 No 8 150-53 1 fig [17 refs]

The authors describe a very interesting case of epidemic typhus fever. The patient was an Armenian carpet worker aged 52 years. He gave a clear history of having suffered from a severe attack of typhus fever in South Russia in 1918. Since his arrival in Switzerland in 1939 he had never been in contact with a known or suspected case of typhus fever, and he had never been infested with lice. The authors state that apart from a few cases of laboratory infection and some isolated cases among refugees who had arrived from Germany during the incubation period, there had been no typhus fever in Switzerland since 1940. The possibility of infection through handling infected articles in the course of the patient's occupation was excluded because imports of all such goods from the east had ceased for several years.

The attack occurred in June 1945. It was moderately severe and lasted 14 days. The rash was pronounced, it extended to the palms and soles and became haemorrhagic.

The Weil-Felix reaction was negative on the 12th day, but was positive 1-640 on the 19th day when the complement fixation test was also positive at a titre of 1-1,280 with epidemic typhus antigen and at a titre of 1-320 with murine-typhus antigen.

The authors conclude that the case strengthens the hypothesis of ZINSSER that infection may persist for many years in the body after an attack of typhus fever and may cause a greatly delayed relapse. This conclusion seems to suggest that the authors incline to the view that infection can be carried over between epidemics by persons who harbour latent infection of this kind, but they emphasize the fact that nothing is known with certainty as to the manner in which infection persists during the inter-epidemic periods. They discuss the other theories dealing with the carry-over of infection and dismiss the view that inapparent infections are responsible. They consider that the dried-house-faeces theory is based on the unreliable evidence of what happens in purely artificial conditions. Even the theory of maintenance of infection in rat fleas in the form of murine rickettsiae is admitted to be purely speculative so long as there is no experimental evidence that *Rickettsia mooseri* can undergo transformation into *R. prowazeki*.

No mention is made of an attempt to isolate the rickettsia from the present patient. The complement fixation test is accepted as supplying proof that *R. prowazeki* was the causal agent.

John W D Megaw

BERGER E. & BRZEZINSKI S Chemotherapie der Fleckfieber-rickettsien-intoxikation und ihre Aufhebung durch p-Aminobenzoesäure. [The Chemotherapy of Typhus-Rickettsia Intoxication, and the Inhibitory Effect of p-Aminobenzole Acid (on the Antidotal Action of Sulphonamides)] *Schweiz med Woch* 1946 Mar 2 v 76 No 9 173-4 [17 refs]

The authors have already shown that the toxic effect produced in white mice by the intraperitoneal injection of lung substance heavily infected with typhus rickettsiae can be greatly diminished by subcutaneous injections of 2 mgm. of sodium sulphathiazole or Na 3,4-dimethylbenzoylsulphanilamide ("Irgafen"). No significant antimicrobial action was observed.

They now show that *p*-aminobenzoic acid inhibits the antitoxic action of the sulphonamides.

All the mice used in the experiments received similar heavy doses of highly toxic rickettsial suspensions prepared from the pneumonic lungs of infected mice and injected into the peritoneal cavity. The control mice in each set of experiments received these doses and were not otherwise interfered with in any way.

In the first series of experiments three lots of mice were given the standard doses of toxic material, but sodium sulphathiazole had been added 40 minutes before these were administered. All of 10 mice inoculated with this material survived for 48 hours and also all of 10 mice to which 1.0 mgm. of *p*-aminobenzoic acid had been given subcutaneously in addition. But the third lot of mice to which larger doses of 10 mgm. of *p*-aminobenzoic were given, had 7 deaths among 10 animals within 24 hours.

There were 15 deaths among 20 control animals within 48 hours.

In the second series of experiments a course of subcutaneous injections of Irgafen was started 2½ hours before the injection of the toxic material. Five doses of 2 mgm. each were given over a period of 24 hours. Among 12 mice treated in this way there were 3 deaths all within 18 hours. In another lot of 12 mice treated in the same way but with the addition of five doses of 2 mgm. each of *p*-aminobenzoic acid, given subcutaneously within five minutes of the doses of "Irgafen," there were 10 deaths within 48 hours.

Of 20 control mice 19 died within 48 hours.

In the third series of experiments *p*-aminobenzoic acid was given by the mouth, in 5 doses of 3 mgm. each to 11 mice to which the toxic injection was given one hour after starting the same course of Irgafen as was employed in the second set of experiments. 10 of these mice died within 48 hours as compared with 5 deaths among 12 mice to which Irgafen had been given but to which no *p*-aminobenzoic acid was administered.

Of 20 control mice in this series 16 died within 48 hours.

The authors conclude from these findings that *p*-aminobenzoic acid abolishes the antidotal action of sulphonamides on the rickettsial toxins.

They also discuss the theory that the action of the sulphonamides is on the metabolism of pathogenic organisms and conclude from their own and other workers' observations that this theory is based on inadequate evidence, and therefore cannot at present be accepted as a working hypothesis in experimental chemotherapy.

John W. D. McGow

CAVAILLON A. BERNARD L., BOYER & DELECOURT. La lutte contre le typhus exanthématique en France après la libération. [The Campaign against Exanthematic Typhus in France after the Liberation.] *Bull Acad U/I* 1945 v 129 Nos. 36, 37 & 38 637-42, 1 fig.

The authors state that typhus fever did not occur in the expected widespread epidemics after the return of about two million persons from Germany in 1945 and explain why this was so.

The first alert was in February when 97 cases occurred among 2,500 Russian soldiers in a camp at Courme. This epidemic was promptly controlled. A comprehensive plan of action was prepared at a conference of the Ministries, of War, Public Health and "P.D.R." A sanitary barrier was set up on the left bank of the Rhine from Switzerland to the North Sea and provision was made for the inspection and disinfection of every person who crossed the river from the East. Before this had been organized a number of persons had returned to France within the incubation period, so that steps were taken to

ensure the notification and segregation of everyone who had a suspicious febrile attack within 15 days of returning to his home.

The number of cases verified in April 1945 was 31 in May it rose to 229 in June it fell to 51 and in July to 5 In August September and October no cases were reported.

The regional public health centres throughout France were supplied with 250 tons of DDT powder [strength not specified]

The Departments specially affected were the Seine (183 cases mostly in Paris) the Bas-Rhin (20) the Rhône (16) and the Nord (15) Paris was the main clearing centre to which most of the repatriated converged before returning to their homes

Three-fourths of the patients were political deportees 50 of these came from Buchenwald 22 from Mauthausen 10 from Neuengamme 9 from Dachau and the rest from 14 other camps.

The success of the campaign was attributed chiefly to dusting with DDT which was carried out in Germany on the Rhine in the Frontier Reception Posts in Paris and in the Provinces. The percentage of louse infestation among the patients in the Paris hospitals fell rapidly from 44 in the middle of April to about 13 in the middle of May Only 21 secondary cases were detected. Making the fullest allowance for the fact that seasonal climatic conditions were exceptionally unfavourable for the spread of infection from July till October it seemed certain that disinfection was remarkably successful. This success was all the more definite because little was done to disinfect clothing or to administer vaccine though the authors consider that both of these measures ought to have been adopted.

John W D Megaw

VIEL, B & ROMERO H Dos epidemias de tífus exantemático [Two Epidemics of Exanthematic Typhus (In South Chile)] *Rev Med Chile* 1945 Oct. v 73 No 10 847-54 2 figs

The interesting feature of these two epidemics is the striking contrast between the ease with which one of them was controlled by treating all the huts in the affected area with a 10 per cent. DDT powder and the elaborate organization needed to deal with the earlier one which occurred before DDT was available.

John W D Megaw

ECKE R. S GILLIAN A. G SNYDER, J C., YEOMANS A. ZARAFONETIS C. J & MURRAY E. S The Effect of Cox-Type Vaccine on Louse-Borne Typhus Fever An Account of 61 Cases of naturally occurring Typhus Fever in Patients who had previously received One or More Injections of Cox-Type Vaccine. *Amer J Trop Med* 1945 Nov v 25 No 6 447-62, 1 fig [26 refs]

The authors working with the U.S.A. Typhus Commission made a careful study of the effects of an ether-extracted Cox type vaccine in a large group of persons exposed to infection by louse-borne typhus in the course of their work at the Cairo Fever Hospital. The standard of protection aimed at was a course of three doses of vaccine at weekly intervals followed by single stimulating doses at intervals of 4-6 months. Persons exposed to the same risk, who had refused vaccination, served as controls. Every possible care was taken to avoid the fallacies incidental to observations of this kind. Complete data are recorded in tabular form for 61 patients who contracted typhus after receiving varying numbers of doses of the vaccine the only death was in the case of a man aged 35 years who had received a single dose three days before the onset of the illness. The chief findings are shown in the following table —



## Tropical Diseases Bulletin.

Doses of Vaccine	Interval since last dose	Number of patients	Average length of illness (days)	Severity of attack				Fatal
				Very mild	Moderate	Severe	Very severe	
3 or more	21 or more days	28	10½	21	5	0	0	0
2	21 or more days	7	12	4	3	0	0	0
1	21 or more days	11	12.7	2	8	1	0	0
1	Less than 12 days	17	15	4	5	4	0	1
1		10	15½	0	5	2	0	3
Nil				1	12	18	5	8
Other hospital patients treated at same time and of same age group		44						
No Vaccine								

A careful statistical study showed that the disturbing influence of age could be excluded. The findings suggested that administration of the vaccine during the incubation period might lessen the severity of the illness so that a campaign of vaccination is recommended even during an epidemic. There was no evidence of a falling off in the efficacy of the vaccine up to 325 days after the last dose, but the data do not justify conclusions with regard to the duration of the protection.

John W. D. Megaw

MOOSER, Hermann Die Beziehungen des murinen Fleckfiebers zum humanen Fleckfieber  
This book is reviewed on p. 611

BOVENTER, K. & FISCHER, R. Ueber das Rattenfleckfieber (endemisches gutartiges murines Fleckfieber) in Sizilien [Rat Typhus (Endemie, Mild, Murine Typhus) in Sicily] *Deut. Tropenmed. Zeitschr.* 1944 Jan. 1 v. 48 Nos. 1/2, 1-7

The authors describe four cases of rat typhus seen in Sicily in December 1942, and the first six weeks of 1943. The diagnosis was made on the strength of the symptomatology, the epidemiological conditions of occurrence, and the positive Weil-Felix reaction. Animal-inoculation experiments could not be carried out. Italian observers had already reported the occurrence of 31 cases of the disease in Sicily.

The authors classify the typhus fevers as louse typhus, rat typhus, tick typhus and mite typhus. They state that the transmitting vectors of rat typhus are the rat and the rat flea. [Presumably they regard the name flea typhus as unsuitable because they accept the view that infection is often acquired through ingestion of food contaminated by the urine or faeces of infected rats, but even assuming that this view is well founded the more familiar name murine typhus would be preferable.]

John W. D. Megaw

PASCAL H. & CRUZ E. Considerações sobre rickettsioses nos municípios de Itaparituba, São João da Boa Vista e São José do Rio Pardo (Contribuição ao estudo das Rickettsioses) [A Study of the Rickettsial Diseases of the Municipalities of Itaparituba, São João da Boa Vista, and São José do Rio Pardo (South Brazil)] *Arquivos de Hig. e Saúde Pública* São Paulo 1945 June v. 10 No. 24 297-304 English summary (5 lines)

The authors have made a diagnosis of flea-borne Typhus Murinus or Brill's disease in six cases in São João da Boa Vista in 1944 and in seven cases in

São José do Rio Pardo since 1941. The Weil-Felix reaction (*Proteus* OX19) was positive in high titres and the epidemiological conditions were in keeping with the diagnosis. Tables are given of all the cases in which positive Weil-Felix reactions were observed in both localities since 1939. In the former four persons gave positive reactions with *Proteus* OXK in 1939 at titres of 1-100 to 1-200 and two other persons reacted with *Pr* OX19 at titres of 1-100 and 1-400 respectively. No other positive reactions occurred till 1944 when all the reactions were of the OX19 type at titres of 1-1 600 and over. In the latter area during 1939 six positive reactions were observed. They were (1) OXK 1-100 (2) OXA 1-200 (3) OXA 1-800 and OX19 1-400 (4) OXA and OX19 1-1 600 each (5) OXK 1-100 and OX19 1-400 (6) OX19 1-100. In 1940 the OX19 reactions greatly predominated, and in the later years no OXK reactions have been observed. [This change in the type of the serological findings is curious. It may even give rise to a suspicion that the *Proteus* strains used in the tests were not always true to type.] John W. D. Megaw

SMADEN J. E., RIGHTS F. L. & JACKSON Elizabeth B. Studies on Scrub Typhus. I. Soluble Antigen in Tissues and Body Fluids of Infected Mice and Rats. *J. Exper. Med.* 1946 Feb 1 v 83 No 2 133-46 [17 refs.]

The studies described in this paper have already been reported in summarized form to the U.S.A. Typhus Commission in August 1944 and March 1945.

Two strains of typhus rickettsiae were studied, Imphal No 8 and a Calcutta strain. These had been passed 6-7 times through rabbits and afterwards were maintained by transfer through yolk sacs. Material obtained from yolk sacs of the 12th to 43rd passages was used to inoculate mice and white rats by the intravenous route and cotton rats by the intracardiac route. The doses given caused death on the 4th to 6th day. Heart blood, pleural fluid, lung and spleen tissues of the infected animals were used in the experiments for the detection of the antigens. The methods of preparation are described, they included grinding of the tissues and extraction with ether.

Antigens obtained from the tissues of mice infected with one or other strain gave the same complement-fixation responses as sera of mice immunized with either strain and cross-immunity tests also showed that the strains could not be distinguished from each other.

Antigen prepared from the lung tissues of infected mice was found to be strictly specific when used in complement-fixation tests. The reactions with scrub-typhus sera were positive; those with epidemic and endemic sera were completely negative.

Serum and pleural fluid from mice that had died on the 4th to the 6th day contained the specific antigen, but when the mice had survived for longer periods, as happened after intraperitoneal inoculation, no appreciable amount of antigen could be detected, presumably because of a low rate of production and of the longer time that was available for the formation of neutralizing antibodies.

By high-speed centrifugation of the ether-extracted tissue suspensions it was found that the antigens were present almost exclusively in the soluble form in the supernatant fluid. The authors suggest that the antigens had been released because of damage to the rickettsial bodies in the process of grinding and extraction.

Although the sera of the infected animals were much less infective than their tissue suspensions they contained appreciable amounts of complement-fixing antigens which persisted in undiminished quantity after high-speed centrifugation and therefore appeared to be in soluble form. Heating the

serum and pleural fluid to 56°C. for half an hour did not destroy the antigens. In ether-extracted tissue suspensions there was a variable rate of diminution of the antigen during storage at 5°C.

John W D Megaw

BROWNING J S RAPHAEL M KLEIN E F & CONLEY, A. Scrub-Typhus.  
*Amer J Trop Med.* 1945 Nov v 25 No 6 481-92 2 charts. [12 refs.]

This study is based on 173 cases of scrub typhus admitted to hospital from various places in the New Guinea Archipelago. There were six deaths, all of which occurred among 16 patients admitted from one locality within a period of three weeks. Infection was thought to have occurred while they were sitting on the only patch of grass in the neighbourhood.

The Weil-Felix (OAK) test was of great value in diagnosis but a titre of 1-80 was seldom reached before the ninth day and in one group of patients from an isolated area the reaction was uniformly negative.

Some of the chief features of the disease were as follows (figures in brackets are percentages) —Headache (92) orbital pain (82) chills or chilly feeling (47) eschar (80) usually on the legs or in the axillae maculo-papular rash (35) and subconjunctival haemorrhage (33). Leucopenia was not frequent but relative lymphocytosis was usual. A pulse rate over 120 per min. usually indicated the presence of a complication.

Among 112 patients examined by electrocardiography about a month after the onset, 18 were abnormal but 40 per cent. of these became normal within a month.

The chief complications in the acute phase were (in percentages) impaired hearing (30) pulmonary (17) abdominal distension (10) epistaxis (5) arthralgia (4) and retinal haemorrhage (2). In convalescence there were seven cases of psychoneurosis and six of neurocirculatory asthenia both of these conditions were regarded as due largely to anxiety resulting from reading or hearing reports of permanent damage to the heart. There were four cases of myocardial damage, but the authors believe that there will be no permanent sequelae.

John W D Megaw

MEXDELL, T H. Scrub Typhus Fever (Tsurugamushi Disease) in New Guinea. Report of 75 Cases. *Amer J Med. Sci.* 1946 Jan v 211 No. 1 9-22.

This study of scrub typhus is based on 75 cases of which two were fatal, seen in North New Guinea during the months August September and October 1944.

The incubation period was known in only one case in which it was 21 days. The area where the infection was contracted consisted of grass and scrub land 58 of the cases occurred during the first half of the period, before the site was cleared, and after three months the disease ceased to occur.

The incidence of the chief features was as follows figures in brackets are percentages —The eschar (86) was single except in seven patients the usual sites were the axilla, scrotum and groin. The macular rash (78) was on the trunk and limbs to a lesser extent on the face. Adenopathy (85) was most pronounced in the glands associated with the eschar. Splenomegaly occurred in 37 cases. Conjunctivitis (71) affected the palpebral conjunctiva, from which it extended with diminishing severity towards the cornea. In many cases there were subconjunctival haemorrhages. Deafness (35) was transient except in one case. The central nervous system was specially involved in nearly half the cases. One patient had a severe post typhus psychosis with ultimate recovery and two others had a temporary psychosis in convalescence.

lasting a few days Rickettsial pneumonitis or bronchitis occurred in 38 cases (51) Hypotension was a constant feature. Leucopenia was usual with relative lymphocytosis

The Weil Fehx test (OAK) was carried out in 34 cases it was negative in three in eight the titre was 1-40 and in 23 it was 1-80 or over

At autopsy in the two fatal cases a vasculitis with perivasculitis was the chief feature the vessels chiefly affected were the smaller ones of the brain lungs and heart and the chief changes were in the reticulo-endothelial system

There was a pronounced tendency to haemorrhages.

Sodium chloride (6 gm daily) was given as a routine therapeutic measure.

The convalescent period ranged from one to six months Stress is laid on the need for reassuring the patients to prevent disabling neuroses.

John W D Megaw

AGRESS C. M & EVANS E R Clinical Survey of Eighty-Six Cases of Scrub Typhus. *Bull U.S Army Med Dept* 1946 Feb 15 No 2 163-9

The authors studied 86 cases of scrub typhus of which 79 occurred among Chinese soldiers in Assam and North Burma between November 1943 and September 1944 The case-fatality rate was 10 per cent. The average duration of the illness before admission to hospital was seven days The clinical picture was not unusual in any important respect

The percentage incidence of some of the chief features was as follows headache 86 backache 73 cough 40 deafness 28 eschar 78 lymphadenopathy 94 conjunctivitis 65 remittent type of fever 60 intermittent type 40 termination by lysis 100 and positive *Proteus* OAK agglutination, 1-40 or over 80

A definite rash was seen in 31 per cent of the patients including 10 in whom there was only generalized erythema the types of rash observed were macular 18 cases maculo-papular 12 erythematous 10 and papular 1 [Presumably in a number of the cases the rash was partly macular and partly maculo-papular] The rash extended to the face in three cases the palms and soles were never affected. There was often a short recrudescence of fever after the temperature had been normal for two or three days.

The leucocyte count ranged from 1 900 to 26 400 per cmm. the average count in the 1st week was 9,800 in the 3rd week it was 12 100 The percentage of lymphocytes ranged from 9 to 75 the average was 29 per cent in the 1st week, and 43 per cent. in the third.

Among 19 cases tested in the 2nd week the OAK reaction was positive (1-25 to 1-1 600) in 11 in the 3rd week it was positive in 13 of 18 cases tested in the 4th week it was positive in 27 of 30 cases tested and in the 5th week it was positive in all the 10 cases tested.

Sulphathiazole was given to 16 patients but it only added to their discomfort. Plasma given to 10 patients caused no striking improvement

John W D Megaw

ANDREW R. Fluid Balance in Scrub Typhus. *Med J Australia*. 1945 Dec. 15 v 2, No 24 432-4

The interesting observations described to this paper are based on a study of 11 severe cases of scrub typhus in North Queensland. The infection in 10 of the patients was contracted on the same day Sudden diuresis occurred on the 10th-16th day of the disease in 10 of the cases and on the 32nd day in the remaining case. The average daily fluid intake before diuresis occurred was 97 oz and the output [presumably urinary] was 44.7 oz. On the first day of

diuresis the average output rose suddenly to 96.4 oz. though the intake had risen by only 20 per cent. to 116.7 oz. The diuresis occurred on the average about three days before the temperature became consistently less than 99°F and it was accompanied by a striking improvement in the general condition of the patients though at first sight they looked worse because of the sudden disappearance of the oedema that had masked the pronounced degree of anaemia.

No obvious cause could be found for the diuresis: in a few cases the blood pressure had been observed before and after the event, but no significant difference was detected, traces of albumin were found in the urine of three patients but there was never anything approaching nephritis. The serum proteins were within normal limits in the cases tested from this point of view.

The findings are regarded as reinforcing the warnings against further deranging the fluid balance in patients with scrub typhus by intravenous injections: more than five or six pints of liquid daily by the mouth are considered unnecessary.

The climate of the hospital area was hot and humid, the altitude was about 2,000 feet.

[Climatic conditions must be taken into account in estimating a suitable fluid intake.]

John W D Megaw

DONEGAN E. A. Ocular Findings in Tropical Typhus (Tsutsugamushi or Japanese River Fever). *Brit. J. Ophthalm.* 1946 Jan v 30 No. 1 11-19

The eyes of a total of 101 cases of tropical typhus were examined, and the ocular changes may be summarized as follows—In the acute stage the conjunctivae are generally hyperaemic without involvement of the cornea, clearing about the 14th day. The fundi typically show a disk in which there is pathological hyperaemia with an overlying central vitreous haze with its margins blurred in at least two quadrants often accompanied by swelling. The vessels show little or no change even in patients with marked cerebral symptoms as they give no suggestion of venous stasis. The hyperaemia disappears once the acute stage of the disease is over and the fever has subsided. The vitreous haze then clears about the end of the third week. The last sign to disappear is the marginal blurring which may persist in some cases for more than a month after the subsidence of systemic signs of the disease. The interpretation placed on the ocular signs is that of a vascular upset not a neural or neuroglial involvement by invasion of the nerve tissues by the rickettsial bodies. There appears to be only very slight reaction to the organism which would explain the absence of post-neuritic changes due to fibrosis of the optic nerve and retina. It is not understood why toxic substances which have done so much harm to renal and hepatic tissues should allow the more delicate cells of the brain and retina to escape obvious permanent damage.

E O G Kirwan

IRONS E. N & ARMARUST C. A. Jr. Relation of the Weil-Felix Reaction to the Clinical Course of Tsutsugamushi Disease. *Bull. U.S. Army Med. Dept.* 1946 Jan. v 5 No. 1 85-84 8 charts. [16 refs.]

The authors studied the Weil-Felix (OXK) response in 74 cases of tsutsugamushi disease of which seven were fatal. The conclusion is stated as follows—“The incidence of Weil-Felix reaction was inversely proportional to the severity of the illness: 94.5 per cent. of the moderately severe, 90 per cent. of the severe, but only 29 per cent. of the fatal cases showed a Weil-Felix reaction during the course of the disease. [This conclusion is hardly justified by the facts supplied: the only significant figure is that relating to the fatal cases

but the day of death is stated in only two instances in one of which death occurred on the 15th day and the reaction was positive while in the other death was on the 16th day and the reaction was negative. Seeing that the delay in the appearance of a positive reaction averaged 17 days and in some cases was up to 24 days there is no justification for regarding the negative reactions among the fatal cases as being comparable with those among survivors. Also the classification of the cases as 'severe' when the duration of the fever was 18 days or more and as 'moderately severe' when it was less than 18 days irrespective of all other considerations is open to criticism.

A really valuable feature of the paper is the set of seven charts which show the relationship between the rise and fall of the titres and the course of the illness.]

John W D Megaw

BENGTSON Ida A Apparent Serological Heterogeneity among Strains of Tsutsugamushi Disease (Scrub Typhus) *Pub Health Rep* Wash. 1945 Dec 14 v 60 No 50 1483-8

The complement fixation titres of sera of animals and human beings infected with different strains of *Rickettsia orientalis* were found to vary greatly according to whether a homologous or heterologous antigen was used in carrying out the test. Most of the experiments described were done with Karp (New Guinea) and Gilliam (Assam-Burma border) strains. A Seerangayee strain (Malaya) was used in some of the tests it had been found more virulent for guinea-pigs than the other two strains whereas the Gilliam strain was the most virulent to chick embryos in yolk-sac cultures. The virulence of an Imphal (Assam) strain for chick embryos was exceptionally low and altogether great differences in virulence were found.

A typical example of the variations in the complement fixation titres is as follows.—The serum of a guinea-pig infected by the Gilliam strain gave a titre up to 1-2 048 with Gilliam antigen and up to 1-8 with Karp antigen. So also a Karp-strain serum gave a titre of 1-250 with Karp antigen of 1-4 with a Gilliam antigen and of 1-16 with a Seerangayee antigen.

The sera of patients who had been accidentally infected by Karp and Gilliam strains gave correspondingly different responses according to whether a homologous or heterologous antigen was used. In every case the response with the same antigen was at a titre which was at least 100 times greater than that given when the other antigen was used.

The Karp and Gilliam antigens were used in tests of sera from patients suffering from epidemic endemic and Rocky Mountain-spotted-fever infections and in every case the reaction was negative.

Several groups of serum from cases of tsutsugamushi disease in the Pacific area were tested all gave positive fixation against the Karp or Gilliam antigens.

TOPPING has already shown that cross immunity exists between guinea-pigs that had been infected with the Karp Gilliam Seerangayee and another strain it remains to be found whether there is an association between the fixation titre and the degree of immunity [See the comment on the paper by ZARAFONETIS above]

John W D Megaw

CHARTERS A. D Tick-Typhus in Abyssinia *Trans Roy Soc. Trop Med & Hyg* 1946 Feb v 39 No 4 335-42 1 chart. [13 refs]

This is claimed to be the first description of tick-borne typhus in Abyssinia though the author mentions that the Army Pathological Laboratory Service in its *Current Notes* for December 1941 stated that the disease occurs there and that the vector is *Rhipicephalus sanguineus*.

reducing sugars. In the course of an investigation on plasma substitutes one of the authors observed that pyrogenic solutions of gelatin were rendered non-pyrogenic by heating with potassium permanganate or hydrogen peroxide. Further work has shown that if pyrogenic solutions are heated at 100°C. for 60-120 minutes in the presence of 0.1 M hydrogen peroxide their pyrogenic properties are abolished and at 0.01 M concentration are decreased. The change is not due to alteration of pH.

The authors suggest, therefore, that treatment with hydrogen peroxide may be of practical use so long as the hydrogen peroxide does not adversely affect other constituents of the solution and so long as the amount used is not sufficient to destroy the pyrogens and leave a deleterious excess.

Charles Wilcocks.

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### BACILLARY DYSENTERY

ELSON K. A. PEPPER, D. S. & FORRESTER, J. S. The Treatment of Bacillary Dysentery in Chinese Soldiers with Sulphaguanidine and Sulphadiazine. *Amer J Med. Sci.* 1946 Jan. v 211 No. 1 103-9 3 charts.

From June to December 1943 334 Chinese soldiers suffering from acute bacillary dysentery were treated in rotation as admitted to a hospital in North Eastern India with (a) a placebo or (b) sulphaguanidine 3.5 gm. four hourly or (c) sulphadiazine 3 gm. initially and then 1 gm. four hourly. The diagnosis was clinical the patients were graded as slightly moderately or severely ill stool specimens were examined and bacteriologically cultured early after admission and a confirmatory bacteriological diagnosis was established in 25 per cent. of the cases which were found equally distributed in the three treatment groups.

The average periods of fever of diarrhoea, and of hospitalization were unaffected by the alternative treatments with sulphaguanidine sulphadiazine or the placebo and the authors consider whether this divergent result from the findings of other workers was due to the late stage at which the cases presented themselves (treatment was begun on the average, 5 days after the onset of symptoms) or to the predominantly mild form of the bacillary dysentery from which most of the patients suffered. They are not convinced that either explanation is the correct one. They observed no toxic effects from sulphaguanidine but the renal complications from the use of sulphadiazine were frequent and, at times, alarming. Two fatalities might have resulted from the latter but for the available facilities for ureteral lavage and it is concluded that, under the climatic and other conditions of this study the dangers of sulphadiazine in the dosage used exceeded those of the disease for which it was given.

A. R. D. Adams

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### AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

REES, C. W. & REARDON, Lucy V. Comparative Yields of *Endamoeba histolytica*-Organism  $\pm$  from Soluble and Insoluble Ingredients of Egg White in Freshly Prepared and Stored Medium. *Amer J Trop Med* 1945 Mar v 23 No 2, 109-14 [14 refs.]

Having shown that good growth of *E. histolytica* can be obtained in a modified LES [Locke-egg-serum] medium in which the whole egg is replaced by egg white enriched with cholesterol and vitamins, the authors attempted to

discover whether the essential ingredient of the egg white was a water-soluble fraction or a heat-coagulable fraction. The egg white was poured into boiling Locke's solution and the coagulum separated by centrifugation. Neither the Locke's solution containing the uncoagulated ingredients nor Locke's solution to which the coagulum had been added were able to replace the Locke's solution and egg white of the modified LES medium. Strangely enough this was also true of the two fractions when combined in a single medium. The operation of separating the two fractions by heat had altered the amoeba nourishing properties of the egg white. Egg yolk also was not a substitute for egg white. In these cultures only a single bacterium (organism *f*) was present and it grew without any difficulty. It was shown that permeable membrane bags containing Locke's solution and organism *f* when inoculated with *E. histolytica* allowed growth of the amoebae when the bag was kept in contact with an egg slant overlaid with Locke's solution in which organism *f* was growing. Presumably amoeba nourishing materials liberated from the egg slant diffused through the membrane in sufficient quantities to permit growth of the amoebae. It was found that though coagulated egg white favoured growth of amoebae when it was confined to the base this was not the case when it was contained in the overlay.

Another result has been the demonstration that early spring or summer eggs or pullet egg white yield a more favourable medium than fall [autumn] or winter eggs. It was found that if medium is stirred it loses its properties if oxygen is absorbed as through a cotton stopper. If the stopper is rubber and the residual oxygen is absorbed by pyrogalllic acid deterioration of the stored medium does not occur. Under these anaerobic conditions of storage ovomucoid diffuses from the egg white base into the overlay with the result that the oxygen free overlay is capable of yielding a good growth of amoebae. The results appear to indicate that fresh egg white base acting in conjunction with organism *f* is concerned in the oxygen potential of the medium. Though the investigation has yielded interesting results it has not shown what fraction of egg white is responsible for growth of the amoebae. C M Wenyon

KERSHAW W E. The Diagnosis of Amoebiasis. *Brit Med J* 1946 Mar 2 305-7

Amoebiasis is acquired much more commonly by Europeans in the East than is generally realized. The seriousness of the infection is not fully appreciated there or in the United Kingdom. Of 300 cases seen in Ceylon one-half were diagnosed after three and the remainder after eight to twelve stool examinations but even this number of examinations cannot be considered as adequate for the detection of every case. Difficulty was experienced in recognizing cysts which were more readily identified after a modification of Faust's method of concentration had been introduced. This primarily had the virtue of freeing cysts from the matter which obscured their identification in fresh faecal material. The author considered that there was a regular rhythm in the appearance of amoebae pre-cystic amoebae and cysts in his cases both acute and chronic. Sigmoidoscopy was not of great value in the diagnosis of clinically latent cases. A R D Adams

SOKOLOFF B. New Aspect in Treatment of Amebiasis. *Rev Gastroenterology* 1945 Nov-Dec. v 12 425 [Summary taken from *J Amer Med Ass* 1946 Mar 2 v 130 No 9 607]

Sokoloff found that lactic acid even in a weak solution of 1 : 1 000 impedes the multiplication of protozoa including amebas. Since ingested lactic acid is



actively absorbed in the small intestine and therefore is of little use in the treatment of infections of the large intestine a special anhydrous form of lactic acid, trilactic was developed. Trilactic dissolves in water slowly and for this reason reaches the colon and cecum without being affected greatly by the gastric juice. Research has demonstrated that trilactic has a therapeutic effect in animals infected with pathogenic bacteria. Rats infected with *Endameba histolytica* were submitted to trilactic therapy. Although they had only a mild form of amebiasis, their stools showed presence of trophozoites and cysts. These disappeared after seven days of treatment with trilactic. The animals seemed to have been completely cured. During the last five years trilactic has been tested on a number of patients with amebic infection. In many instances they received the trilactic treatment after emetine had failed to eliminate completely the pathogenic ameba, or when the patient had experienced a toxic reaction from this drug. In a few instances trilactic was administered after protracted iodine therapy when stools still showed presence of the cysts. Such combined therapy showed the most satisfactory results not only in the complete elimination of the ameba but also in the prompt restoration of the normal bowel movement. Sixty two patients affected with acute and chronic amebic infections have been treated with the anhydrous form of lactic acid known as trilactic. Complete recovery was obtained in 36 improvement in 15 and negative results in 11 patients.

DUNLOP E. E. Surgical Treatment of Dysenteric Lesions of the Bowel among Allied Prisoners of War in Burma and Thailand. *Brit Med J* 1946 Jan. 28 124-7

Dysentery levied a heavy toll amongst prisoners of war working on the Thailand-Burma railway. Numerous prisoners suffered simultaneously from dysentery, malaria, tropical ulcer and gross malnutrition and the medical officers had to contend with shortage or complete absence of specific amoebicidal drugs, lack of facilities for microscopy and for proper nursing and feeding of the patients and with the action of the Japanese in forcing men with established dysentery to continue working. In consequence many of the patients developed very severe lesions with a tendency to become chronic and emetine-resistant, or to relapse almost immediately on the cessation of treatment. In the acute phase often with 60 or more motions daily there was gross cellulitic swelling of the large bowel with tumour formation in the caecal region, sometimes leading to sloughing, perforation and peritonitis. In the chronic cases scarring, thickening and fibrosis were often found in the caeco-appendicular region at operation. Structure formation after sloughing was met with principally in the rectum. Drugs, in so far as they were available, had been administered to the patients in quantities normally curative: bowel washes of saline, gumme, yatrien, silver nitrate etc. had also been used but had given disappointing results owing to the intense irritability of the inflamed bowel. The failure of medicinal treatment and the wretched plight of the patients led to a trial of surgical measures for the relief of pain and tenesmus. In the more acute cases appendicostomy proved most effective, permitting thorough flushing of the large bowel, whilst in the cases of long standing with a grossly damaged colon, ileostomy was the method of choice as it afforded complete rest to the large bowel. Appendicostomy was performed in 8 cases, ileostomy in 14, caecostomy in 1 and partial resection of the colon in 3 cases. Three deaths occurred amongst the ileostomy patients and one after resection of the right half of the colon in a patient who had suffered from an amoebic abscess of the liver together with a carcinoma of the hip. Six of the eight appendicostomy patients regained good health, with negative stools. In one case the fistula has been closed and in another

it was allowed to close spontaneously. Seven of the ileostomy cases have regained their health eating a normal diet and doing light work, and needing only a weekly colon wash-out. The others are improved. Only one case so far has been closed, after two years rest of the bowel in other cases closure was deferred until after evacuation from Thailand. The need for a post-operative course of emetine is stressed, as there is a danger of spread of amoebic infection to the abdominal wall.

[In the same number of the *British Medical Journal* is a paper by Capt. S. S. PAYILLARD on Medical Experiences in Siam (this *Bulletin* 1946 v 43 489) which gives a vivid picture of the terrible conditions under which medical officers had to work in Siam.]

CLARK R. H. P. & DUTTA D. K. Pneumo-Peritoneum in the Investigation of the Right Costo-Hepatic Area. *Indian Med Gaz.* 1945 Nov v 80 No 11 554-6 6 figs on 4 pls

Pneumo-hepatography is a valuable diagnostic aid in determining whether a lesion lies above or below the diaphragm or whether distortion of a clearly visualized diaphragm is due to deformity of the liver itself. The authors have employed the procedure on 35 occasions without ill effect except in the case of one elderly patient with a rigid emphysematous chest who suffered pain and dyspnoea for six hours. Emphysema should therefore be added to cardiac insufficiency and an acute infection as a contraindication to pneumo-peritoneum. The methods of inducing pneumo-peritoneum have been reviewed by MAXFIELD and McILWAIN (*Radiology* 1944 v 42 436). ASTLETT and JARMAN (*Lancet* 1945 v 1 304) report fatalities in two cases of pulmonary tuberculosis one after the 4th and the other after the 14th peritoneal refill. RICHARDS (*Lancet* 1945 v 1 414) commenting on these adds a record of another fatality due to air embolism on the fourth day after pneumo-peritoneum. Carbon dioxide may be used more safely than air as it is rapidly absorbed but on this account the X-ray examination would have to be made immediately after the injection. MAXFIELD and McILWAIN have injected 3 000 cc. or more of this gas into the peritoneal cavity.

The authors give an account of their technique using a pneumothorax apparatus connected to an 18 or 20-gauge needle. They found 350 to 500 cc of air sufficient in Indians of light build to separate the diaphragm and liver and they fluoroscoped the patients in the standing position 4 to 8 hours after its introduction. Both the liver and the spleen may be visualized as the gas accumulates under the diaphragm by putting the patient on one side or the other its distribution may be varied.

Notes are given of five illustrative cases where pneumo-hepatography materially assisted in the diagnosis of obscure liver conditions and reproduction of 14 X-ray pictures illustrates the salient features of these cases. The authors conclude that pneumo-hepatography is a valuable and safe aid to diagnosis.

KARL W. Hepatic Abscess Secondarily Infected  
*Indian Med Gaz.* 1945 Sept. v 80 No 9 451-2.

A. R. D. Adams  
Penicillin Treatment.

A British officer aged 35 was transferred to the author's care on 20th November 1944 with a history of illness of about one month's duration which had been diagnosed at first as pneumonia and diaphragmatic pleurisy and had been treated with sulphapyridine 26 gm. in 6 days. Soon afterwards amoebic hepatitis had been diagnosed and ten injections of 1 grain of emetine hydrochloride had been given from 29th October to 7th November. On 30th October the liver margin reached to the level of the umbilicus and X-rays showed

elevation of the right side of the diaphragm the patient had irregular fever and his leucocyte count was 17,200 cells of which 86 per cent. were polymorphonuclears. Sterile fluid was aspirated from the right pleural cavity. Next day October 31st, thin red fluid containing *Extemoebe histolytica* was aspirated from the upper part of the right lobe of the liver.

By 10th November the liver dulness had decreased to the level of the 4th anterior intercostal space above and to three fingerbreadths below the costal margin his irregular temperature had settled and the leucocyte count was 7 400. On 17th November fever recurred, liver dulness reached upwards to the 2nd rib and X-rays showed right pleural effusion. Next day 240 cc. of haemorrhagic fluid were aspirated and 150 cc. on the following day (November 19th).

On transfer to the author's care on 20th November liver dulness extended to the 4th rib and to 1 in. below the level of the umbilicus the leucocyte count was 13,200. A second course of 12 injections of emetine hydrochloride was given from 22nd November to 5th December his general condition improved and he remained afebrile. On 4th December 20 cc. of chocolate-coloured pus were aspirated from the right chest it contained pus cells but was sterile. The liver dulness now reached to the 7th rib in the mid-axillary line and to three fingerbreadths below the costal margin.

On 7th December he had a rigor followed by irregular high fever no malaria parasites were found in the blood. On 11th December he had severe right shoulder pain the leucocyte count was 16 400 with 76 per cent. of polymorphonuclears. Emetine bisulphate iodide, 3 grains daily was given without benefit. On 15th December X rays showed a large cavity with a fluid level at the 4th rib his general condition was grave.

On 18th December two pints of pus were aspirated and 200 000 units of penicillin in 90 cc. of saline were injected into the cavity the pus was thick, grey and very foul-smelling and in cultures showed *Bacterium coli*, *Staphylococcus albus* and *Bact. alkaligenes*. Sulphathiazole 6 gm. daily was given from the 18th to the 25th December a total of 40 gm. On 20th December the leucocyte count was 20,000. Fever persisted after the course of sulphathiazole and on 29th December X-rays showed a fluid level at the 5th rib. Next day 2½ pints of thick yellow sterile pus without foul odour were aspirated and 200,000

units of penicillin in 150 cc. of saline were injected into the cavity. On 28th December the abscess cavity was opened and drained by a de Pezzer catheter. Capacity was estimated to be 5 pints and about 3 pints of light-yellow, odorless, sterile pus were evacuated. By 8th January 1945 the size of the cavity was 6 ounces and 3 weeks later it was 2 ounces, while after a further 2 weeks there was no discharge and the wound had almost healed.

The author concluded that "either penicillin was the chief sterilizing agent or the combined effect of the two drugs was a mutually reinforcing one and amounted to more than the sum of the separate actions." J. F. Corson

## RELAPSING FEVER AND OTHER SPIROCHAETOSIS

SERGEANT E. Pe  
cervical abscess  
Years 1  
1944

ence de *Spirochaeta hispanica* pendant trois ans dans le  
3e Note. [The Persistence of *Spirochaeta hispanica*  
of a Guinea pig] 1st Pasteur d'Algérie  
-8 1 fig

used  
just as in previous  
291], and recent  
on the  
in which

the brain of a guinea pig was found to be infective 36 months after spirochaetes had disappeared from the circulating blood. The author's experiments also show that this "Chiffalo" strain of spirochaetes isolated in 1933 still preserves the same virulence after 313 passages in guinea pigs

*E. Hirdle*

TUCKER, W. A. L. A Report on the Treatment of Tick Relapsing Fever with Sodium Penicillin. *East African Med J* 1946 Jan. 23 No 1 13-18

The author refers to the marked increase of tick-transmitted relapsing fever (*S. duttoni*) in East Africa, especially in the Western and Buganda Provinces of the Uganda Protectorate and to the comparatively unsatisfactory results of arsenical treatment in this disease. Accordingly 36 typical African cases were selected from admissions to hospital and treated with sodium penicillin. The 36 cases comprised 16 adult males 9 adult females (4 pregnant) and 11 children. All showed spirochaetes in the blood before treatment was started, and were given doses of 5 000 to 25 000 units of sodium penicillin every four hours usually intramuscularly but in four cases intravenously. A total dosage of at least 300 000 units seemed to be necessary to effect a cure. For comparison 19 patients were treated with either neocarsphenamine or sulpharsphenamine.

In the penicillin series the average time for the temperature to return to normal was 23.4 hours and the blood films became negative in an average of 20.1 hours. The series treated with arsenicals took an average of 16.7 hours for the temperature to return to normal and 17.4 hours for the blood to become negative.

Three arsenic resistant cases were treated with penicillin and all relapsed. Relapse occurred in 27.7 per cent. of all the penicillin cases, and in 31.5 per cent. of those treated with arsenicals.

The author concludes that penicillin does not seem to be more effective than arsenical preparations in the treatment of this strain of relapsing fever but that penicillin is the drug of choice when jaundice is a prominent symptom.

*E. Hirdle*

## YAWS

IBARRA PEREZ, R. & GONZALEZ PRENDES M. A. La frambesia en Bayamo (Frambuesa, pian, yaws o bubas) [Yaws in Bayamo (Cuba). *Rev. Sifilografía, Leprología y Dermatología* Marianao, Cuba. 1945 Dec. v 2 No 4 206-18]

Yaws it is said was practically unknown in Cuba before Professor Castelló diagnosed it in 1932 in three children of one family in Sagna de Tánamo. Since then the number seen has increased, particularly in the Province of Oriente. Others say that it has been present in Cuba since 1893 introduced from Haiti.

A Commission to study the question was constituted in 1937 and that year 274 cases were diagnosed 133 of them in Baracoa and 103 in Sagna de Tánamo. By the following year the total was 1 125 of which 191 were in Baracoa, 111 in Sagna de Tánamo and 567 in Bayamo. In 1941 99 new cases brought the Bayamo figure to 666 and by 1944 there were 845. It has been generally stated and believed that yaws is largely a disease of the black races but the authors' investigations go to show that under the same conditions the white races are every bit as susceptible. In fact of these cases 71.9 per cent. were whites 19.2 per cent. were half-castes and only 8.9 per cent. were negroes.



VARRA PEREZ R. & GONZALEZ PRENDES M A Lepra en Cuba (Leprosy in Cuba.) *Rev Sifilografia Leprologia y Dermatologia* Marianao Cuba. 1945 Dec. v 2 No 4 252-72 [29 refs.]

The subject dealt with is comprised in three papers concerned with different aspects of the question. The first on Leprosy in Havana, is largely historical of the epidemiological and treats of the founding of Havana in 1519 its geographical position and general topography. From available records it would seem that leprosy was known to exist there in the latter part of the sixteenth century and its introduction is ascribed to colonizers and slaves. In 1681 the children's Hospital for lepers was founded the attendants being Sisters of Mercy. The town now comprises 43 Wards and lepers may be found in all parts. The incidence of leprosy is estimated as 0.47 per mille inhabitants—320 cases in a total population of 676,376. Control is maintained and those who are properly looked after in their homes are segregated contacts are kept under surveillance with a view to protecting the healthy public from contamination.

In the second paper gives more statistical information on the general prevalence of leprosy in Cuba. The area of the island is given as 114,524 sq km. 2,539 lepers are registered and it is thought that the actual figure is for the year about 4,000. Havana itself has the highest incidence 5.7 cases per 100 population. Pinar del Rio the lowest 0.48. Taking the figure of 4,000 as fairly correct the incidence of leprosy in Cuba would be on an average 3.49 per 100,000 sq km.

The third contribution deals with the incidence of leprosy in Cuba relative to the population. In this paper the authors revert to the figure of 2,539 cases previously given which with a population of four and three-quarter millions gives a rate of 5.3 per 10,000. Of the total cases 592 are in hospitals and 1,947 free to move about. In the provinces of Camaguey and Cienfuegos the proportion of ambulant cases is 5.15 per 10,000. Havana has 3.82 and Pinar del Rio fewest with 1.66. After giving the above figures the authors reiterate the statement of the preceding paper that the probable number of lepers in Cuba is about 4,000.

H Harold Scott

CASTRO PALOMINO J & ALFONSO Y ARMENTEROS J La lepra en el dispensario Saenz. Estadística de los casos atendidos durante dos años. [Statistics of Lepers attended at the Saenz Dispensary (Cuba) 1943-45.] *Rev Sifilografia Leprologia y Dermatologia* Marianao Cuba. 1945 Dec. v 2 No 4 249-51

Together 119 new cases have been seen in the 2 year period. Sixty were males & 59 were females. As regards type of disease, 65 were lepromatous 22 tuberculoid 12 non-characteristic and 20 unclassified. It has been the policy to examine them all bacteriologically to make histological and biological investigations and to estimate the blood sedimentation rates. Seventeen have been transferred to other dispensaries leaving 102 of whom 3 have died and 30 have disappeared and cannot be traced. As regards race, 96 were whites 6 negroes 16 half-castes and one a Chinese. Two were under 10 years old 10 were in the second decade, and in succeeding decades to the seventh the figures were 24 34 22 12 and 12 there were three patients over 70 years of age.

H Harold Scott

PEREIRA, P. C. R. As leprolinas Souza Aranzo—seu emprego—resultados em comparação com a reação de Mitsuda. [Tests with Souza Aranzo Leprolins compared with Reactions to Mitsuda's Lepromin.] *Mem. Inst. Oswaldo Cruz* 1945 v 42, No. 1 217-21

The author has tested the leprolins of Professor de Souza Aranzo (see this *Bulletin* 1945 v 42, 1010-12) in two groups of lepers: one (28 in number) no longer harbouring the bacilli, the other (29) with bacilli, and has compared the results with those obtained from Mitsuda's lepromin. Positive reactions were evidenced by erythema of varying extent lasting for a few days and then gradually fading; rarely the erythema would appear late, some 8-12 days after injection of the antigen. Nodules varying in hardness with tissue reaction might also appear and occasionally there was suppuration with loss of tissue. In both groups three failed to give any reaction to the leprolins. In the first group the non-bacilliferous, 15 reacted to all the antigens and all 25 to antigen 4. In the second (bacilliferous) group one only reacted to all four antigens but all the 28 did so to antigen 4.

As regards Mitsuda's lepromin reaction this was tested in the nonbacilliferous group only. A table gives the results in each of the 28 patients. These may be summed up by saying that they were not in accord: a patient might give a positive to leprolin but negative to lepromin.

H. Harold Scott

CHORINE V. Traitement des lésions oculaires de la lèpre. [Treatment of the Ocular Lesions of Leprosy.] *Bull. Soc. Path. Exot.* 1945 v 38, Nov. 9/10 255-71. [21 refs.]

The treatment of the ocular complications of leprosy is discussed by Chorine. He points out that the eyes are frequently attacked by the disease but that the statistics collected by workers in different countries are contradictory. As samples of these he quotes the figures of ROGERS and MUIR (this *Bulletin* 25 v 22, 256) for India at 5 to 10 per cent, those of PINKERTON (*Arch. Ophthalmology* 1927 v 56, 42) in Hawaii and of JEANSELMER (this *Bulletin* 34 v 31, 754) in Indo-China at 100 per cent, those of FIDOSSEV and PAVLOV in Soviet Russia at 62 per cent. It is the opinion of most authorities that the longer the duration of the disease the commoner the ocular complications, that the nodular type more frequently causes involvement of the eyes than the neural type and that ocular complications of leprosy, including blindness, are much less frequent in warm than in temperate and cold climates.

The author advocates the use of sulphonamides parenterally and recommends the following solution:—

Acetamide	80 gm.
Septophix [sulphonamide]	15 gm.
Distilled water	100 cc.

The injections are painful and are given around the circumference of the orbit. A preliminary injection of 4-5 cc. of 1-2 per cent. Stovaine is given into the orbit, and then the sulphonamide solution is injected into the anaesthetized area. Both eyes are treated simultaneously and one or two injections of 2 to 5 cc. are given into each orbit. Small doses are given at first to test the reaction of the patient and the injections are carried out once a week. The author reports remarkable improvements in the ocular complications as a result of this treatment.

E. O'G. KIRWAN

PEREIRA O de Lodiola. Contribuição ao Estudo do Tratamento da Leprea segundo os resultados obtidos em 10 anos de Terapêutica Antileprotica na Leprosaria Central do Gêa.  
This book is reviewed on p 609

## HELMINTHIASIS

VISHNIEVSKAYA S M [Helminthological Examination of Sewage, Soil and Vegetables from the Bezindov Fields Manured with Sewage] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 4 14-18 [In Russian]

After quoting several Russian papers on the contamination of vegetables by helminth eggs the author records his examination of sewage water from the main and secondary canals used to irrigate the Bezindov fields and also of the sediment from these. He also examined washings from vegetables (tomatoes cucumbers and cabbages) grown on these fields. The observations were made in 1937 and 1938. Water samples were taken from the canals in bottles containing 48 litres these stood for two days before the sediment was examined by the author's modification of the method of LEIV (no reference to this method is given). Soil was taken from the surface of both irrigated and non-irrigated areas and also at a depth of 12 cm in samples of 200 to 250 gm. Vegetables were washed twice and both washings were centrifuged, the sediment after centrifugation being examined by the method of Lem.

The author found in the sewage water from the irrigation canals eggs of those species of helminths which have been found in the impure sewage water of the Kharkov district namely *Ascaris Trichuris Trichostrongylidae* and a cestode referred to as the dwarf-chain [some other Russian authors mean by this phrase *Hymenolepis nana* but unless the Latin name is given it is difficult to be sure what species is meant]. The majority of the eggs found were those of *Ascaris* and the following figures refer to these only. More eggs were found in 1 litre of the water from the main canals i.e. 22-40 per litre than in the same amount of water from the secondary canals i.e. 14-18 per litre. The author claims that this fact demonstrates the part played in dehelminthization by the canals. In the sediment from the main canals there were 3 to 10 eggs per gm and in the soil from the irrigated areas there were only 0.5 to 1 egg per gm. Thus the passage of the water along the canals at a speed of 22 cm per second removes the author claims 50 per cent of the eggs. The eggs of *Ascaris* found were not usually morphologically altered they were segmenting and, under favourable conditions most of them developed until infective larvae were formed in them. In the surface layer of the soil of the irrigated areas up to 70 per cent of the eggs of *Ascaris* were morphologically unchanged and 23 to 30 per cent of them were deformed. Isolated eggs when they were incubated, developed until they contained infective larvae. In ploughed soil of the irrigated areas the author found that from 65 per cent (in 1937) to 80 per cent. (in 1938) of the eggs were morphologically unchanged and these developed under favourable conditions until they contained infective larvae. In soil from the irrigated areas taken at a depth of 12 cm 55 per cent. of the eggs of *Ascaris* were morphologically unchanged but these did not develop under favourable conditions. In the soil from areas irrigated only before they were ploughed isolated eggs of *Ascaris* were found whose external appearance suggested that they were morphologically unchanged.

In sediments obtained after washing vegetables grown on the Bezindov fields the author found an average of 0.3 to 1 *Ascaris* egg per gm of sediment.



Isolated eggs of *Ascaris* were found on the vegetables grown on fields irrigated with sewage during the summer but no eggs of any helminth were found on vegetables grown on land irrigated with sewage water during the autumn or winter nor were any eggs found on vegetables from areas irrigated only before they were ploughed. [Cf VASILKOVA this Bulletin 1945 v 42, 569]

G. Lafage

ALF S. [Contamination of Soil by the Eggs of Helminths by the Burial of Sewage.] *Ud Parasit & Parasitic Dis* Moscow 1945 v 14 No 4 18-22. [20 refs.] [In Russian.]

After reviewing the literature on this subject the author records his observations on three shallow pits each with a capacity of 1 to 1.25 cubic metres in which faecal matter was buried. Two pits were in sandy soil and the third was in clay soil. The faeces contained 1 000 to 2 000 eggs per gm. and in 65 per cent. of these eggs active embryos developed under favourable laboratory conditions. These 65 per cent. were eggs of *Ascaris*. [The author does not state whether eggs of other species were found.] Samples of soil were taken with a soil borer around each pit at horizontal distances of 0.5, 1, 2 and 3 metres from the walls of the pits and at vertical depths from the bottoms of the pits of 0.5, 1.25 and 2.5 metres. These samples were taken in different directions at right angles to each other. Similar samples were taken from control plots distant 8 metres from pit no. 3 and 5 metres from pit no. 2. Each sample consisted of not less than 1 kgm. of soil. The eggs were recovered from the samples by a modification of the method of SPORNIAK [no reference to this method is given] samples of 300 gm. of soil being thus examined. The results showed that there was no infection of the soil at horizontal distances of 0.5 to 3 metres from the walls of the pits or at vertical depths from the bottoms of the pits of 2.5 metres (i.e. 1 to 1.25 metres below the bottoms of the pits)

G. Lafage

COCKBURN C. Ocular Cysticercosis Cellulosa. Report of a Case of Parasite in Vitreous. *Brit J Ophthalmol*. 1946, Feb v 30 No 2, 65-74 5 figs. (1 a coloured pl.).

COLE G. Hydatid Disease in Victoria. *Health Bull* Melbourne 1945 Jan-June Nos. 81-82, 2178-83 1 map Addendum I II & III pp 2189-92, 2 figs.

Hydatid disease was made notifiable in Victoria in 1926 and from then to the end of 1944 278 cases have been notified, 136 of them in the Western Health area 52 in the Central, and 43 in the North-western areas. That is 44.6 per cent. of notified cases have occurred in an area less than one-eighth of the State, with 4.4 per cent. of the State population it is practically certain that several escaped notification. The disease is in the main, restricted to the sheep-country and investigations at various abattoirs showed that from 28.7 to 71 per cent. of the sheep killed were infested with hydatids. Also of 24 dogs whose faeces were examined, 8 were passing adult *Echinococcus granulosus* these animals are commonly fed with uncooked offal from the slaughterhouses. Preventive measures are simple easily understood and easily applied, and a vigorous campaign is suggested the appointment of a committee to investigate the problem more deeply and the adoption of a publicity campaign the preparation of a wall-sheet showing the life history of the worm and the distribution of it to all schools exhibiting posters of similar design in abattoirs and at railway stations the wide distribution of leaflets and securing publicity by Press co-operation. The article mentions five other cestodes which may

infest dogs namely *T. hydatigena* (intermediate *Cysticercus tenuicollis*) *T. pisiformis* (*Cysticercus pisiformis*) *T. serialis* (*Coenurus serialis*) *T. ovis* (*Cysticercus ovis*) and *Dipylidium caninum* the last only infesting man

There are three addenda to the main article the first gives details of the investigation of dogs referred to above the other two are pamphlets of general information issued by the Medical Officer of Health and the Commission of Public Health. The last contains an excellent illustration of the small intestine of a dog heavily infested with the cestode. *H Harold Scott*

LASNIER, E P & CASSINELLI J F Diagnóstico de quiste hidático hialino (no roto) del pulmón mediante la inclusión de esputos. [Diagnosis of Unruptured Hydatid Cyst of the Lung by Examination of the Sputum.] *An Facul de Med Montevideo* 1945 v 30 No 12 903-45 14 text figs & 5 coloured figs on 1 pl. [32 refs.]

This long article pleads for examination of the sputum in patients with unruptured hydatid cyst of the lung. The authors show with illustrative photomicrographs and a coloured plate how by suitable staining (particularly by Best's haematin and carmine method) fragments of the cyst wall and minute cocco-bacillary bodies can be seen and diagnosis made. All this is gone into in much detail for which those interested must consult the original. *H Harold Scott*

HUNTER G W III & WORTH C B Variations in response to Filariform Larvae of *Ancylostoma caninum* in the Skin of Man. *J Parasitology* 1945 Dec. v 31 No 6 366-72 1 fig. [16 refs.]

Reports of the effects of penetration of the human skin by filariform larvae of *Ancylostoma caninum* have varied some record a transient papular dermatitis others deeper penetration and creeping eruption.

Two volunteers submitted themselves to infection on the right forearm with 1 000 or more filariform larvae of *A. caninum*. In both cases the immediate reaction was acutely inflammatory after that their reactions differed sufficiently to warrant separate description.

The first volunteer felt an itching and the area in 45 minutes became erythematous in 48 hours urticaria and papules were numerous and on the third day induration and tenderness and sulphadiazine was prescribed. Except for a slight rise of temperature less than 1°F on the 2nd and 3rd days there was no systemic disturbance. Subsequently at intervals increasing in length, there occurred attacks of transient urticaria. Biopsy revealed no parasites and the stools examined up to 180 days after infestation remained negative for ova. Leucocytes on the 3rd day totalled 9 900 per cmm. with eosinophiles 2 per cent. the highest eosinophilia was 9 per cent. among 8 850 leucocytes on the 85th day.

The second volunteer had an allergic history personal and familial. His immediate reaction to the application of the larvae was less intense on the 3rd day there was spreading inflammation with some superficial tenderness and papules were becoming vesicular. Burrows were visible on the 4th day. On the 7th there was deep induration of the forearm with aching pain and pitting oedema. Several times during the ensuing months there were renewed burrowings and localized swellings. But whereas with *A. brasiliense* the burrows are continuous with the site of entry of the larvae i.e. the larvae possess invasive properties against a poorly resistant host in the case of *A. caninum* there is local arrest and the larvae penetrate deeper and rise to the surface again at a distance (in the case of this experimental subject, some

7-8 in. from the site of entry) No ova were seen in the faeces at any time. In this volunteer the blood showed an eosinophilia of 28 per cent. on the 29th day in a total leucocyte count of 12,600 and of 15 per cent. on the 72nd day in a total of 12,000 after which the eosinophilia fell till the 181st day when the number rose to 1 072 (or 8 per cent. of a total leucocytosis of 13 400) from 522 (8 per cent. of 6 700) on the 120th day. It may be concluded that the human subject may vary constitutionally in his ability to arrest the invasion of a parasite which may be considered uniform within its species."

H. Harold Scott.

MELWIDSKY H. The Surgical Complications of Ascariasis. *Acta Med. Orientalia (Palestine & Near East Med J)* 1945 Nov v 4 No. 11 370-84 28 refs

An account of the surgical complications of ascariasis illustrated by clinical details of 17 cases met with during six years surgical practice in Jerusalem. The most common complication is intestinal obstruction of which there are four varieties (1) mechanical, (2) spastic, (3) intussusception (4) volvulus. Five cases of mechanical obstruction all submitted to operation are recorded. two early cases in which the bowel was not opened, recovered and three with gangrenous intestine and peritonitis ended fatally after resection of intestine or ileostomy. Two cases are described in which the obstruction was due to ulcers, in one of these the symptoms passed off after the administration of a spinal anaesthetic the other proved fatal after laparotomy and ileostomy. Intussusception and volvulus of the lower ileum occasionally occur. Three patients with the latter condition were operated on two of whom recovered, in one case after resection of 30 cm. of gangrenous gut and a temporary ileostomy. The mortality of this group of 10 cases was 50 per cent. cases which recovered being those in which the symptoms were of only one to two days duration.

Perforation of the bowel may take place through areas of inflammation or ulceration or through suture lines postoperatively. A case of persistent duodenal fistula after gastrectomy for duodenal ulcer is described, in which an *Ascaris* was eventually expelled through the fistula, with subsequent healing of the wound. Appendicitis may of course occur in infested subjects but cases are met with in which it appears to be directly due to the irritation caused by the parasite entering the appendix. two such cases are cited, both of which recovered after appendicectomy.

Acute abdominal symptoms suggesting perforation of a duodenal ulcer may be caused, and two patients sent to hospital with this diagnosis were spared operation because in one case vomiting of some worms led to immediate improvement and in the other the fact that the patient had had two similar attacks during the previous 18 months for the first of which a laparotomy had been performed and only *Ascaris* infestation found, suggested the true diagnosis.

The bile and pancreatic ducts may be blocked by the worm migrating up the common bile duct, setting up cholangitis, cholecystitis and abscess of the liver all of which have been recorded. One of the author's cases arrived in hospital with a diagnosis of empyema of the gall-bladder but here too the vomiting of worms led to investigation and a correct diagnosis.

The differential diagnosis is discussed, but stress is laid on the imperative necessity of surgical intervention in the presence of acute abdominal symptoms and signs without waiting to see the effects of anthelmintic treatment. If a non-urgent abdominal operation has to be performed in an *Ascaris*-carrier pre-operative anthelmintic treatment is advisable.

W. L. Harnett

ALEXANDER A E & TRIM A R. The Biological Activity of Phenolic Compounds. The Effect of Surface Active Substances upon the Penetration of Hexyl Resorcinol into *Ascaris lumbricoides* var *suis* *Proc Roy Soc Ser B* 1946 Feb 12, v 133 No 871 220-34 7 figs. [27 refs.]

This paper must be read in original if it is to be fully appreciated.

The authors have devised a method of measuring quantitatively the effect of surface-active substances (sodium cholate sodium oleate and cetyl trimethyl ammonium bromide (C.T.A.B)) upon the penetration of hexylresorcinol into the nematode *Ascaris lumbricoides* parasitic in pigs. Parallel measurements have been carried out on the interfacial activity of solutions of the substances named against an inert mineral oil Nujol which is a pure high boiling paraffin. The work should be read in conjunction with the work of TRIM [this *Bulletin* 1944 v 41 596] ROGERS [*ibid* 1945 v 42 299] and the other authors quoted.

The action of all three substances was markedly similar and differed only in degree. When a fixed concentration of hexylresorcinol was used (0.025 per cent.) the soap in dilute solution accelerated the penetration of the drug the maximum acceleration being in the order sodium cholate < sodium oleate < C.T.A.B. High concentrations of the soaps however completely inhibited the penetration of hexylresorcinol. The soaps alone penetrated *Ascaris* only very slowly if at all. The soap and the hexylresorcinol molecules associate at an interface forming a labile complex of increased surface activity. The authors suggest that the biological activity of hexylresorcinol as measured by its rate of penetration of the cuticle of *Ascaris* is determined by the interfacial activity of this mixture and that when soap micelles are present the drug distributes itself between the micelles and any other interface present such as oil/water or *Ascaris*/water. Thus the maximum biological activity occurs at the critical concentration for micelle formation because this has maximum interfacial activity. At high soap concentrations the hexylresorcinol is held mainly by the soap micelles so that the biological activity is diminished ultimately it is diminished to zero because the soaps alone penetrate so extremely slowly. It has been possible to calculate from the data provided by the use of C.T.A.B./hexylresorcinol mixtures a theoretical curve for the biological activity of hexylresorcinol which agrees well with the results of experiment. The authors discuss the possible bearings of these results upon the anthelmintic activity of hexylresorcinol *in vivo* and also upon the action of drugs in general (e.g. the action of soaps together with phenols upon bacteria). The authors say that it may be quite feasible by adjustment of the relative amounts of drug and soap to control not only the intensity of biological activity but also the duration at any desired level up to the optimum. With drugs that have undesirable effects on the host this clearly is of great value.

G Lapage

HARRIS J S & SUMMERS W A. A Concentration Method for demonstrating *Microfilariae* in Blood. *Amer J Trop Med* 1945 Nov v 25 No 6 497-8

Four cc. of blood are taken from a vein and put into a tube containing 0.01 cc. of heparin solution (Liquemin Roche-Organon Inc. 1 ml. contains 10 mgm of purified heparin). 4 cc. of a 2 per cent. aqueous solution of saponin are added and mixed with the blood. When haemolysis is complete 6 cc. of the mixture are centrifuged for 10 minutes at 2,000 r.p.m. The supernatant fluid is drawn off leaving 0.1 cc. in the tube and this is spread on a slide and examined with a low power of the microscope. If desired it can be stained afterwards.

The authors found this method superior to other concentration methods

J F Corson.

AUGUSTINE D. L. & LHERISSON C. Studies on the Specificity of Intradermal Tests in the Diagnosis of Filariasis. *Amer J Hyg* 1946 Jan., v 43, No 1 38-40

Earlier work has suggested that intradermal tests done with antigen derived from *Dirofilaria immitis* of the dog has value for diagnosis of filariasis of man. The authors quote for example TALLAFERRO and HOFFMAN [this Bulletin 1931 v 28 214] FAIRLEY *ibid* 1932, v 29 427] DICKSON HUXTINGTON and EICHHOLD *ibid* 1944 v 41 303 MICHAEL (*ibid* 1956). But later work by WRIGHT and MURDOCK *ibid* 1954, and HUXTINGTON (*U.S. Nat. Med. Bull.* 1945 v 44 707) has given irregular and uncertain results. (See also ZARROW and RIFKIN below) Positive reactions ascribed to cross reaction with other nematodes especially intestinal species have been obtained in a large percentage of subjects who showed no clinical symptoms of filariasis and negative reactions ascribed to desensitization have been obtained in persons with acute severe symptoms of Bancroftian filariasis. The authors thought that this lack of specificity of the test might be due to sensitization by repeated exposures to species of filarid nematodes which do not infest man. Adult filarid nematodes are common in frogs lizards birds and mammals. These adults are markedly host specific and there are as many (or more) species of filarid nematodes as there are species of land vertebrates. It is very likely that filarid nematodes are the commonest helminth parasites of land vertebrates in regions where *Wuchereria bancrofti* is endemic.

The microfilarial larvae of these species however are less specific to their intermediate hosts. They can develop in many arthropods especially in mosquitoes. The life-histories of the species not parasitic in man have not yet been worked out. We can expect that they follow the usual pattern shown by *Dirofilaria immitis* of the dog. The microfilarial larvae of *D. immitis* can develop in more than 20 species of mosquitoes belonging to three genera. Its possible intermediate hosts include the usual vectors of *W. bancrofti* and of human malaria. Effective transportation to man of infective larvae of non-human filariae seems unquestionable and, in all probability this is a very frequent occurrence. It is also very probable that these microfilarial larvae which enter man are destroyed in his skin as the infective larvae of the hookworms of dogs and cats and the cercarial larvae of avian and rodent schistosomes are. But repeated infestations of man with these microfilarial larvae can be expected to provoke a potent immune reaction.

The authors therefore studied the specificity of skin tests done on rabbits with antigens made from filarid nematodes which are not parasitic in man namely *Dirofilaria immitis* of the dog *Setaria equina* of the horse *Listosomoides carini* of the cotton rat and *Agrofilaria columbigallinae* of the ground dove. Adult nematodes of these species were washed in running water and then given several baths of distilled water before they were dried over sulphuric acid in *vacuo* for 2 to 3 days. The dried nematodes were ground up and extracted for 3 days in physiological saline containing 1/10,000 merthiolate. After centrifugation the supernatant fluid was used as antigen. Dilutions were made on a dry weight basis and all tests were done on rabbits about 1 year old.

Each of four rabbits was first immunized by subcutaneous injections, on eight occasions of 1 cc. of antigen diluted 1/1,000. On the tenth day after the last injection the intradermal tests were done by injection into a hairless region of the skin of the back of 0.2 cc. of antigen. Control tests were done with physiological saline containing merthiolate. All the antigens were also tested on normal rabbits. A reaction was considered positive when the diameter of the weal produced by the antigen exceeded that produced by the saline, by 3 mm. or more.

The four immunized rabbits were all positive to dilutions of 1 1 000 and 1 8 000 of each of the antigens. The tests done with the 1 1 000 dilutions were the first to appear and the last to fade they were more prominent and were positive 2 hours after the injections. By this time the weals caused by both specific and the non specific antigens varied from 30 millimeters in diameter to 50 by 70 millimeters for antigens in a dilution of 1 in 1 000. The largest weals were produced by the *D. immitis* antigen in a rabbit immunized with antigen from *V. columbigallinae* of the ground dove. This weal disappeared 18 hours after the injection as did also the weal produced by *Setaria equina carinus* the reaction produced by the specific antigen from *Litosomoides carinus* of the cottonrat was however still present at this time. Dilutions of 1 8 000 of the antigens produced milder reactions. After 2 hours the weals had a diameter of 15 to 30 mm and after 18 hours they were not conspicuous. The authors say there was no marked erythema or oedema except in all the tests with *Dirofilaria immitis* antigen in 1 in 1 000 dilution. Erythema and oedema were particularly prominent in the specific tests. All the reactions were inconspicuous or had disappeared after 18 to 30 hours. All the controls were negative. The duration of the sensitivity was not determined. The authors state that their experiments afford no direct evidence that infestations with the microfilarial larvae of filariids not parasitic in man can produce sensitivity in man but claim that their work shows clearly that the extracts of the filariid species used caused an immune response indicated by skin tests whether the antigen was specific or not. They therefore feel justified in supposing that (a) non human filariid nematodes can influence the serological reactions of man and (b) many hitherto unexplained false positive skin reactions to *D. immitis* antigen are due to responses produced by filariid nematodes which are not parasitic in man.

ZARROW M & RIFKIN H. Observations on the Specificity and Clinical Use of *Dirofilaria immitis* Antigen in the Diagnosis of Human Filariasis (*Wuchereria bancrofti*) *Amer J Med Sci* 1946 Jan. v 211 No 1 97-102 [18 refs]

Reviewing the literature on this subject the authors recall that KING [this *Bulletin* 1945 v 42 304] suggested the following three methods for the diagnosis of filariasis — (1) Microscopical demonstration of adult filariae by means of biopsy. The present authors agree that this method is certain but it takes time involves surgical removal of lymph nodes and perhaps the removal of several of these if the first ones removed are negative [see below] and it is not applicable to a field survey. (2) Demonstration of microfilariae in the peripheral blood. To this method the present authors object that nobody has yet demonstrated microfilariae present in the blood of United States soldiers although they are abundantly present in the blood of natives of the areas investigated. In the present study moreover no microfilariae were found in the blood of the white subjects studied although repeated examinations were made both of fresh smears and by the concentration method of KNOTT [this *Bulletin* 1940 v 37 304]. (3) Demonstration of calcified filarial nematodes by Roentgen ray techniques [see O'Connor this *Bulletin* 1930 v 27 986]. The present authors state that it has not yet been shown that these techniques have any diagnostic value. They therefore decided to use a skin test.

A review is given of the literature up to 1944 on intradermal tests with antigen derived from *Dirofilaria immitis*, *Wuchereria bancrofti* and *Litosomoides carinus*. [The papers reviewed have been abstracted in this *Bulletin* see for example the summary of Recent Abstracts on Helminthiasis this *Bulletin*]

## Tropical Diseases Bulletin

1945 v 42, 670] The present authors tried to define —(1) a dilution of the antigen at which false intradermal positive reactions due to intestinal nematodes can be eliminated (2) the sensitivity of subjects suffering from filariasis to the antigen. It was possible also to compare the results of the intradermal tests done on some subjects with those of biopsies done on the same subjects.

The antigen was made from *Dirofilaria immitis* by a modification of the method of HARRINGTON reported personally to the authors by MICHAEL. These were freed from blood by intravenous injection of magnesium sulphate and adult dogs were killed by intravenous injection of acetone. The nematodes were removed from their hearts. They were then given several washes in running water followed by three changes of acetone. The nematodes were then dried in an incubator at 37°C for 12 hours by which time they were thoroughly dry. The authors found that if this temperature was exceeded, the antigen lost potency. The dried nematodes were ground up and the powder was kept in the refrigerator as stock from which fresh antigenic extract was prepared each month. The extract was made by making a 1 per cent suspension of the powder in physiological saline which was constantly stirred for 2 hours at 37°C, and then filtered through a Sinter filter. Phenol was added to a concentration of 3 per cent. Thus 1 100 extract was diluted to 1 200, 1 2,000, 1 4,000, 1 8,000 and 1 16,000. One contaminated batch of extract was re-filtered, and it was found that this process caused a loss of potency a fact which was also reported by KING (loc. cit. above). As a control, a fragment of the dog's heart was given the same treatment as the nematodes and diluted 1 2,000. The tests were done by injecting 0.05 cc. of antigen intradermally into the volar surface of the forearm. One arm received the control and the 1 200 and 1 2,000 dilutions, the other received the other dilutions. Results were read after 24 hours. The authors took as a positive at their height, and also after 30 minutes. The authors compared with hookworm response a definite increase in size of the wheel as compared with the control together with erythema of 2 cm. diameter or more.

There were 65 subjects free from clinical filariasis but infested with hookworm and *Strongyloides stercoralis*. No positive reactions with dilutions above 1 2,000 were obtained in these subjects, with the exception of one who had herpes zoster as well as hookworm disease. *Ascaris lumbricoides* and *Enterobius vermicularis* control heart extract and the authors therefore, feel justified in ruling him out. They conclude that a dilution of 1 4,000 does not give cross reactions due to the presence of intestinal helminths. WAGGOTT and MURDOCK (this Bulletin 1944 v 41, 1051, obtained cross reactions with *D. immitis* antigen at a dilution of 1 4,000 but they injected 0.1 cc. of the antigen, twice the amount used by the present authors).

The authors tested 91 subjects who showed clinical symptoms of filariasis. Of these 83 (91 per cent) gave positive reactions to at least one of the dilutions used. In a controlled group of 18 subjects who had no history of having served in an area in which filariasis is endemic but who showed no clinical signs or symptoms of filariasis 11 did not react to a 1 200 dilution of the antigen, 5 gave positive reactions to this dilution, and 2 to a dilution of 1 2,000. At the higher titres none was positive. The authors conclude from their results that a positive reaction at a dilution of 1 4,000 or higher indicates the presence of filariasis. Using this as a basis for interpretation of their results they obtained a positive response in 78 per cent of their subjects. Comparison of biopsies of lymph nodes and skin tests done on the same persons showed that, in a group of 53 subjects 74 per cent. were positive to dilutions of 1 4,000 and 1 16,000 of the antigen, and that biopsies in 60 per cent. of these were positive but in several subjects more than one biopsy was

needed to find a positive gland. In this group 10 showed negative biopsies but positive intradermal tests and further biopsies might have been positive. In three subjects (6 per cent.) the biopsies were positive but the skin tests were negative. A similar finding was also recorded by DICKSON HUNTINGTON and EICHHOLD (this *Bulletin* 1944 v 41 303).

In 55 soldiers all of whom had been exposed to filariasis and some of whom had enlarged lymph nodes but were otherwise free from symptoms positive intradermal reactions were obtained in 71 per cent to dilutions of 1:4000 and 1:16000 of the antigen.

Complete blood counts were done on all those who had filariasis. There were no marked deviations in the number of erythrocytes, haemoglobin, neutrophils or lymphocytes but 25 per cent of the subjects showed an increase in the number of white blood cells to 10000 per cmm. or slightly more. The eosinophils were increased to 34 per cent or more in the whole group of 91 men with clinical filariasis. When only those who gave positive skin tests to dilutions of 1:4000 or higher were considered it was found that 40 per cent had eosinophilia and 15 per cent of these harboured intestinal helminths.

LEEDE W E & JOSEY A I. The Early Diagnosis of Filariasis and certain Suggestions relative to Cause of Symptoms. *Ann Intern Med* 1945 Nov v 23 No 5 816-22

G Lapage

The authors studied 100 soldiers evacuated from various areas of the South West Pacific with filariasis. From only two of these men were microfilariae recovered. The diagnosis in the others rested on (1) a history of residence in an endemic area (2) a history of symptoms suggestive of early filariasis (3) the clinical findings (4) the results of skin tests with filarial antigens and (5) the subsequent clinical course of the condition. There is great variation in the initial symptoms of infections acquired in different localities but those from any one locality are constant. In general however after about one year's residence in an endemic zone an infected man experiences mild generalized aches and pains testicular pains and malaise and a more or less generalized lymphadenopathy and funiculitis develop. Lymphangitis is of diagnostic importance but is not always evident. In early cases microfilariae will only very rarely be found in the peripheral blood.

The immediate evacuation of early cases from the endemic zone will result at least in the temporary subsidence and possibly in the complete disappearance of the disease—it is yet too early to state which with certainty. The available evidence indicates that avoidance of reinfection or removal to a temperate climate or both result in diminution of the frequency and severity of the symptoms and in recession of the physical signs of the infection.

The causation of the symptoms and signs of early filariasis is difficult to explain on the basis of mechanical obstruction by the parasites such as leads to the irreversible changes seen in the later stages of the disease. An inflammatory or allergic tissue response appears a more probable explanation. The sudden onset and evanescent nature of the initial symptoms and signs with an associated eosinophilia suggest an allergic basis for their occurrence.

A R D Adams

GOODMAN A A WEINBERGER E M LIPPINCOTT S W MARBLE A & WRIGHT W H. Studies of Filariasis in Soldiers evacuated from the South Pacific. *Ann Intern Med* 1945 Nov v 23 No 5 823-36 [18 refs.]

This is a report on the investigations made on soldiers repatriated to the United States from the small islands in the South Pacific as early cases of (25)



Bancroftian filariasis. The clinical symptoms and signs of the disease were of minor severity and accord with those described by other American workers.

The authors examined the intracutaneous test (both direct and passive transfer) and the complement fixation test in their series of cases. For these purposes they used antigens prepared from *Dirofilaria immitis* and *Setaria equina* diluted 1/4000 and 1/8000 the antigen controls were similarly diluted preparations of dog and horse protein. In addition a series of non-filarial human controls was subjected to intradermal and complement fixation tests with the same antigens the results are set out in the text and in two tables. Some additional information is given of intracutaneous tests with antigens prepared from *Trichinella spiralis*, *Listomonoides carinii* and *Acarus lumbricoides* in varying dilutions and also to Frei's antigen in view of the importance of differentiating inguinal gland enlargements due to lymphogranuloma inguinale and to filariasis. The undesirability of using antigens in stronger solution than 1/8000 for intracutaneous tests is indicated, and there is a comment on the disappointing degree of specificity of both the intradermal and the complement fixation tests, and their correlation in diagnosis.

The authors conclude with the following summary:—

1 Clinical findings and results of intracutaneous and complement fixation tests in 145 soldiers evacuated from the South Pacific Area because of suspected bancroftian filariasis, are presented.

" 2 Signs and symptoms suggestive of filariasis including lymphadenopathy lymphangitis scrotal edema funiculitis orchitis and varicocele, arose on the average after about 13 months residence in an endemic area.

" 3 The symptoms were, in general, mild and only six patients experienced bouts of acute lymphangitis during the period of study in the United States. No case of elephantiasis occurred. No case of chyluria was encountered.

" 4 Microfilariae were demonstrated in the blood on one occasion in each of four patients (in two of these at overseas hospitals)

" 5 In 47 patients eosinophilia of 4 per cent. or greater was found in eight patients the percentage was 10 or greater

6 Microscopic examination of excised lymph nodes in 19 cases showed only a non-specific inflammatory response ("reactive lymph node"). No adult worms or remains of worms were seen.

" 7 In four of 29 cases roentgenograms of the scrotum showed tiny areas of calcification. However it is not possible to state that such calcification was due to the presence of *W. bancrofti*.

" 8 Direct intracutaneous tests using antigens of *Dirofilaria immitis* and *Setaria equina* in 1/8000 dilution gave positive responses in 84 per cent. of cases as compared with 6 per cent. in a series of 106 control subjects. Of 75 patients tested with 1/200 dilution of *Listomonoides carinii* 77 per cent. gave positive reactions.

9 In passive transfer tests positive responses were obtained to either or both *D. immitis* or *S. equina* antigen in 1/8,000 dilution in 29 per cent. of cases. Of 50 patients tested with a 1/200 dilution of *L. carinii* 46 per cent gave positive reactions.

10 Positive complement fixation tests were found in 95 or 66 per cent., of 143 patients studied. However the complement fixation technique used cannot be considered wholly specific since 16 to 25 per cent. of normal control subjects gave positive tests. It is believed that improvements being effected in the technique of the test will reduce the number of non-specific reactions. There was agreement between the results of the complement fixation tests and the direct intracutaneous tests with *S. equina* and *D. immitis* in 68 and 71 per cent. of patients respectively.

11 No specific treatment was given. Therapy included a liberal diet, reconditioning by means of gradually increasing activity and psychotherapy to allay fears as to possible future complications of the disease. The outlook for the men is considered good because of the relatively short residence in the endemic area and the slight degree of infection.

A R D Adams

WEBSTER E H. Filariasis among White Immigrants in Samoa. *U.S. Nav. Med. Bull.* 1946 Feb v 46 No 2 186-92, 1 graph.

These observations were made on 80 white men and women civilian immigrants in Samoa who had lived there for at least 10 years. The examination consisted largely of questions regarding their histories and circumstances of life in Samoa, signs and symptoms of filariasis and the dates of their appearance. Little importance was attached to the examination of blood films for microfilariae except in special cases and physical examination was limited to cases of elephantiasis. Eleven had also lived in other endemic areas of filariasis but most had not been exposed to infection until they were nearly 30 years of age and had been exposed afterwards for over 25 years.

Symptoms and signs of filariasis were present in 27 of 54 men and 11 of 26 women; the incidence of filariasis was related to the degree or amount of exposure and therefore to occupation (the numbers are small). Figures are given for the average time of appearance of the initial symptoms in males and females and the parts of the body affected. Many gave a history of several attacks of lymphangitis and fever in a year. There were 15 persons with elephantiasis; their ages ranged from 41 (very slight) to 78 (severe); average 64 years and the average duration of exposure to infection was 35 years. The relation to the number of acute attacks is shown in the following table —

*Recurrence of acute symptoms*

Number of recurrences	1-10	11-20	21-40	41-60	over 60
Without elephantiasis	17	2	2	2	0
With elephantiasis	0	5	2	4	4

There was only one case of severe elephantiasis in a trader aged 78 with both arms and both legs affected.

J F Corson.

SCHLOSSER, R. J. Observations on the Incidence of *Wuchereria bancrofti* Larvae in the Native Population of the Solomon Islands Area. *Amer J Trop Med* 1945 Nov v 25 No 6 493-5

Thick blood films taken at various times by day or night from some hundreds of natives of three of the Solomon Islands (Guadalcanal, Malaita and San Christoval) from natives of the Gilbert Islands and of the Fiji Islands were examined for microfilariae of *Wuchereria bancrofti*; the parasites were found in about 20 per cent. Other observations showed that there was a definite periodicity, the night blood containing far more microfilariae than the day blood, the difference in numbers being more marked in natives of the Solomon Islands than in those of the Gilbert Islands.

Some feeding experiments were made in the Gilbert Islands with *Aedes punctulatus punctulatus* and *Aedes punctulatus forsteri*; the microfilariae did not survive for more than 36 hours in the former species and in one only out of 24 of the latter did microfilariae live for more than four days. The author states

that BYRD and St. AMANT have demonstrated that in the Solomon Islands the microfilariae will readily develop to the infective stage in *Aedes punctulatus farauti*.  
J F Corson.

DANGLADE, J. H. & FITZGERALD P. J. Asymptomatic Microfilariaemia in the Caribbean Area. *U.S. Nat. Med. Bull.* 1946 Feb. v 48 No 2 193-201 2 figs. [22 refs.]

Microfilariae of *Wuchereria bancrofti* were found in the night blood of 9 negroes of St. Croix Virgin Islands who gave no history of having had signs or symptoms of filariasis and in whom none could be found on physical examination. In blood taken between 11 and 12 o'clock at night no microfilariae were found in fresh preparations they were seen in stained thin films in 5 and in stained thick films in 7 by the use of a modification of a concentration method (LAWRY) in which 2 cc. of blood were mixed with 10 cc. of 2 per cent. formalin and centrifuged at 2,000 r.p.m. for 5 minutes, and the stained sediment examined, the microfilariae were found in the remaining two patients. [See also O CORCORAN and BEATTY this Bulletin 1939 v 35 761]  
J F Corson

BASTONX, R. N. *Mémoire* A Few Facts about Filariasis for Folks who fear that Filaria-Infected Fellows will fetch Filariae from the Front. *Hawaii Med. J.* 1945 Nov-Dec. v 5 No 2, 69-71

The author's summary expresses completely the contents of the paper —

1. Our cases suffer *simply* an allergic response to worm protein but do not produce microfilariae in the blood at least in demonstrable numbers.

2. It takes years of intensive exposure to develop a good micro-filaria producer. Our men have not had that exposure.

"3. In most of our men the worms will probably all die before the man is desensitized if some should survive they will not be in large numbers nor have sufficient life expectancy to produce secondary micro-filaria-carriers.

"4. Transmission in the homeland will be inefficient also because of the average citizen's aversion to mosquitoes and the extreme paucity of the reservoirs of micro-filariae

"5. Filicidal drugs are known. They can be used if needed, to control transmission. At present they are still in the experimental stage and they appear to aggravate the symptoms of *mémoire*"  
J F Corson

SEN, K. & GHOSE, N. Ocular Gnathostomiasis. *Brit. J. Ophthalm.* 1945 Dec. v 29 No 12 618-26 1 text fig & 1 pl.

A case of *Gnathostoma spinigerum* in the anterior chamber of the eye is described by Sen and Ghose. This is probably the first recorded case of this worm in a human eye. The onset occurred with a dull aching pain on the left side of the nose extending to the left frontal and temporal regions. Swelling of the face then occurred, extending from the angle of the mouth to the roots of the hair and was followed by orbital cellulitis, vitreous and retinal haemorrhages. Later the patient had two attacks of iritis with the development of grey nodules on the iris which completely disappeared, leaving grey depressions. This was followed by two more attacks of iritis with the development of a single pigmented nodule on the iris in each attack. The pigmented nodule completely disappeared, leaving no mark after the first attack. In the second attack, which was the more severe the pigmented nodule was seen to be the worm. The worm was removed at operation and the eye made an uneventful recovery though optic atrophy developed. The habit of the *Gnathostoma* of burrowing through the tissues and migrating from place to place explained all

the signs especially the inflammation which, before subsiding in one place appeared in a contiguous place in quick succession.

The size of the worm was as follows —Length 3.5 mm maximum width 0.41 mm level of maximum width 0.41 mm from the anterior end width of the head 0.25 mm the number of rows of spines on the head bulb was 4. The authors are of the opinion that if the infection took place through the gastrointestinal tract it must have been through swallowing infected *Cyclops* in drinking water. It was not clear how the worm came to the side of the nose from the stomach without causing any sign or symptom. The probable area of its entry into the eyeball from the orbit could be seen as a scar just below the macula.

E O G Kirwan

WHITTIER L. EINHORN N H & MILLER J F *Trichuriasis in Children. A Clinical Survey of Fifty Cases and Reports of Three Cases with Heavy Infection and Striking Clinical Symptoms. Amer J Dis Children* 1945 Nov-Dec. v 70 No 5 289-92.

The authors have analysed the symptoms and treatment of 50 children infested with *Trichuris trichiura* and show that the symptoms may be serious and severe even fatal cases have been reported though none of those under the authors observation died. All 50 were admitted to the paediatric ward of the Gorgas Hospital Ancon during the years 1941-43. Three came from well-sanitised areas of the Canal Zone 22 from overcrowded districts with fair sanitation provided but not fully utilized and 25 from semi-rural communities living amid primitive conditions. The ages of the patients ranged between 12 months and 12 years 28 were under 7 years old 23 were boys 22 were girls. The common complaints were abdominal distress or pain in 9 diarrhoea in 7 blood in the stools in 5 vomiting in 5 fever in 3 but many of the patients were in hospital for other diseases than mere trichuriasis so evaluation of these complaints is not possible. In only one was the pain suggestive of appendicitis whereas SWARTZWELDER had recorded 16 out of 81 in whom the abdominal pain was localized in the right lower quadrant [see this *Bulletin* 1940 v 37 660]. The authors found that the typical history was of diarrhoea of 1 to 3 months duration latterly stools streaked with blood recurrent pain in the abdomen with tenesmus loss of weight and rectal prolapse the worms were often seen by the parents in the wall of the prolapsed bowel. Twelve of the patients had eosinophilia from 5 to 14 per cent. haemoglobin 60-70 per cent. and red corpuscles  $3\frac{1}{2}$ -4 million per cmm. values which compared favourably with those observed in well children in Panama. In the three cases detailed, leucocytosis to 13 500 was present in one only in the others the count was normal and in none of the three was there any eosinophilia in two no eosinophiles are mentioned, only polymorphonuclears and lymphocytes and in the third the differential count [was] within normal limits.

The best treatment in the authors view is hexylresorcinol crystals *per os* combined with retention enemata of hexylresorcinol 1:1 000 but in each of the three cases detailed it will be observed that though general improvement took place the patient on discharge from hospital still had ova of *Trichuris* in the stools

H Harold Scott

NEGHEM R. A. *Epidemiologia de la Triquinosis [Epidemiology of Trichiniasis.] Biológica* Santiago 1944 Sept. No 1 127-40 1 graph. [11 refs.] English summary

The author analyses some of the causes which determine the endemic state of Trichinosis in Chile and indicates frequency attained in rats hogs and in man

"Trichinosis in rats has been stated in Santiago (5%) and in Concepción (7-8%) trichinosis of pigs in the slaughterhouses all over the country in quantities which range from 0-1% in the towns of the North (Antofagasta) up to 6% in some small towns of the South (Quilhue).

In man several Trichinosis epidemics have been discovered during the last 50 years in different towns of Central and South Chile. The author has collected from 1940 to 1943 148 cases of Trichinosis diagnosed mostly by means of Bachman's intradermic reaction. The inquiries on sub-clinical Trichinosis carried out in 294 corpses of the Santiago hospitals by Martink as well as by the author showed a 12.5% infestation with *Trichinella spiralis*. Investigations carried out with Bachman's intradermic reaction in healthy persons showed delayed positive reactions in 5 out of 98 tested individuals (5.2%).

GOULD S. E. An Effective Method for the Control of Trichinosis in the United States. *J Amer Med Ass* 1945 Dec. 29 v 129 No 18 1251-4 3 figs. [Refs. in footnotes.]

This is a useful review of the incidence and control of trichiniasis in the United States in which the author decides that the best and most economical method of controlling this disease in man and hogs is the processing of pork products. No new facts are recorded in the review but some of the facts given are in themselves interesting.

Recent surveys of the incidence of *Trichinella spiralis* in human post mortem material in the United States have shown that the average incidence is 16 per cent. (see GOULD S. E. Trichinosis, 1945 Springfield, Ill. Charles C. Thomas). More thorough methods of examination have shown that the incidence in some areas may be as high as 96 per cent. (see EVANS *J Infect Dis* 1938 v 63 337).

The incidence of *Trichinella spiralis* in hogs in the United States during the last 50 years has not varied from 1.5 per cent. It is possible that each American during life may eat nearly 200 meals of pork infested with *Trichinella*, and it is therefore not surprising that 16 per cent of human diaphragms examined at autopsy contain larvae of *Trichinella*. The morbidity rate from trichiniasis is not definitely known because many infestations are subclinical and, even when symptoms occur they may not be correctly diagnosed but the mortality rate of cases clinically diagnosed is 5 to 6 per cent.

Discussing methods of control, the author says that little progress has been made during the last 50 years in the control of trichiniasis. About 70 per cent. of the pork products made in the United States are made in plants under Government supervision they carry the label "U.S. inspected and passed" but this label on non-processed pork products does not mean that these are free from viable *Trichinella* larvae. Meat packing plants which are under Government inspection must observe Federal regulations for processing pork of the kind usually eaten uncooked and this pork may be expected to be free from viable larvae. But pork prepared in other plants under Federal inspection and all pork not under Federal inspection may contain living *Trichinella* larvae. Sausages are especially dangerous because they are often eaten raw or insufficiently cooked. Because only about 70 per cent. of pork is produced under Federal inspection and because even in these plants it is only the processed pork which can be expected to be free from living *Trichinella* larvae most of the American pork which goes to the kitchen may contain living larvae. Further pork may be put in other foods (meat loaf frankfurters etc.) or bought in shops and, if this is eaten uncooked, it is dangerous. During

recent years there have been numerous lawsuits against packers because of illness or death, with remarkably high awards for the plaintiffs

The incidence in American hogs of 1.5 per cent, is in sharp contrast to the incidence in hogs in Canada (0.57 per cent.) Poland (0.05 per cent.) Germany (0.001 per cent.) and Copenhagen (0.00075 per cent.)

The following methods of control are discussed by the author (1) Destruction of rats. The author considers that pigs rarely eat rats and that although it is wise to exterminate rats they play only a small part in spreading trichiniasis

(2) Education of the public. This is advisable but is by itself of little value.

(3) Skin testing of hogs. The author quotes the opinion of B. SCHWARTZ (*Ann Rep Smithsonian Inst* 1939 413) that this is not a reliable method of determining the incidence in hogs. [But see the flocculation slide test, of SUESSENGUTH and KLINE this *Bulletin* 1946 v 43 360 and the opinion of these authors that their method is a valuable means of determining the incidence in hogs.]

(4) Microscopic inspection of pork. This has proved quite effective in some countries and has been used extensively in Germany. The author concludes that systematic enforcement of it almost eradicated trichiniasis from Germany. Other countries which require microscopic inspection of pork are Denmark, Sweden, France, Argentina and Chile. The United States required it to be done from 1891 till 1906 but only for pork intended for export. Bismarck in 1880 and 1883 prohibited the import by Germany of American pork and even when in 1891 microscopic inspection was instituted in the United States Germany required its reinspection and in 1893 refused to accept the United States certificate that the pork was free from *Trichinella*. [For another discussion of this aspect of meat inspection for Trichiniasis in America see also SCHWARTZ *J Amer Vet Med Ass* 1941 v 98 458] Microscopic inspection was abandoned by the United States in 1906. It has never been applied to pork eaten in the United States. It takes much time although phototrichinoscopes have made it possible to throw on a screen images of several samples of meat from each hog. Further this method may miss infestations when the larvae are young and are not encysted or are in uncalcified cysts because then it is difficult to see them and most hogs in the United States are slaughtered when they are less than a year old, i.e. when any larvae in them are in this condition. Also portions of pork may be examined which do not contain larvae although they are present elsewhere in the hog examined. Microscopic inspection may also give the public a false sense of security.

(5) Elimination of garbage and offal from hog feed and the cooking of garbage given to hogs. Cooked garbage is given to hogs in Canada, England, the Hawaiian Islands and the American States of Kentucky, Oregon and New York. It has been repeatedly advocated and would greatly decrease the incidence of *Trichinella* in hogs. Yet 0.9 per cent of grain fed hogs are trichinized (see SCHWARTZ *J Amer Vet Med Ass* 1938 v 92, 317). This method could not be enforced except upon large breeders. In the American States named above the difficulties of enforcing it have made this method ineffective and in Oregon State people can feed hogs on garbage from their own houses. A large corps of inspectors and others would be needed to enforce this method.

(6) Processing. This measure includes freezing, cooking, smoking, curing etc. Larvae of *Trichinella* are killed by a temperature of 55°C but Federal regulations require that all parts of meat heated to kill these larvae shall be heated to 58.33°C (137°F). Freezing is chiefly used for processing pork. AUGUSTINE (*Amer J Hyg* 1933 v 17 697) showed that raw pork in commercial quantities can be freed from *Trichinella* larvae by a temperature of -35°C (-31°F). BLAIR and LANG (*J Infect Dis* 1934 v 55 95) found that freezing

at  $-17.8^{\circ}\text{C}$ . ( $0^{\circ}\text{F}$ ) for 72 hours killed these larvae. Most of the "deep-freeze" cabinets used in homes give temperatures varying from 0 to  $5^{\circ}\text{F}$  and these can be maintained. This method would cost relatively little and would by killing larvae in any scraps of pork which reach hogs quickly reduce the incidence of trichinosis in hogs and would check its spread in man. *G Lapage*.

PÉREZ ARA A. & PÉREZ VIGUERAS I. Sur un nouveau nématode découvert dans la paupière de l'homme. [On a New Nematode discovered in the Human Eyelid.] *Bull Soc Path. Exot* 1941 v 34 Nos. 4/7 104-7 2 figs.

This note records the removal from the lower eyelid of a Cuban aged 27 of fragments of two unidentified nematodes. About a week before he was seen the patient noticed a very small swelling in his right lower eyelid, which caused him no inconvenience. This swelling appeared to be a non-inflammatory slight thickening about the size of a small pea in the external third of the lower eyelid 1 mm from its free border. It was elastic to the touch and not painful on pressure. The adjacent conjunctiva was normal. When it was removed, the swelling was yellowish white with yellowish white granular contents. From it emerged spontaneously two filiform motile organisms tapering at both ends and resembling worms. These were fixed and examination showed that they were the caudal ends of two female nematode worms both of which were gravid. The anterior ends were not found. One fragment was 7 mm. long, the other 8 mm. The maximum diameter of each was 220 microns. The cuticle was relatively thick with transverse striations only at the caudal extremity although longitudinal striation was evident throughout the length of the fragments and especially on the ventral and lateral surfaces. There were no cuticular spines papillae or lateral alae. The anus was 200 microns from the caudal extremity and the vulva 837 microns from it. The vulval opening was transverse to the long axis of the body. The vagina was cylindrical and relatively large. The uterus contained shelled eggs elliptical in form smooth and easily seen. They measured 20 to 23 microns long by 12.6 to 13.5 microns broad. Some were segmented and some contained embryos. There was no ovjector. No trace of the oesophagus was found in the larger fragment 7 mm long so that the authors concluded that a good part of the anterior end was lacking. The eggs were the authors remark, considerably smaller than those of nematodes parasitic in man. They could not identify the nematodes.

*G Lapage*

## DEFICIENCY DISEASES

SEN P C in collaboration with S. C. SEAL. Types of Oedema Cases seen in a Rural Area in Bengal. *J Indian Med Ass* 1945 Dec v 15 No 3 67-74 & 76 1 sketch map & 1 graph.

Nine cases were studied in considerable detail. There is a general tendency to regard oedema, especially oedema of the extremities and occurring in Bengal as epidemic dropy. The plan of investigation included—(a) General Case Schedule for information of identity history dietetic habits etc. (b) Nutritional Assessment Card with information obtained from physical examination of the patient. (c) Economic Survey Schedule for information as to income, expenditure economic status etc. (d) Diet Survey Schedule, for recording the quantities of various foods taken during a period of 7 days.

Six families were involved. The information mentioned under each of the above is presented in a series of Tables and the upshot was that five of the nine

cases were diagnosed as epidemic dropsy (in two families which used mustard oil containing Argermone oil) three were associated with nutritional deficiencies notably of vitamins A B<sub>1</sub> B<sub>2</sub> and C the ninth was a case of oedema with anaemia secondary to chronic dysentery The last four were infested also with ankylostomes which may have played a part in causing the oedema

H Harold Scott

HUGHES W Fatty Liver and Malignant Malnutrition. [Correspondence.] *Lancet* 1945 Dec. 29 861-2.

In this letter Hughes draws attention to the part played by ariboflavinosis in the aetiology of malignant malnutrition with fatty liver He shows that ariboflavinosis is the most outstanding feature in the epidemiological and clinical pattern of kwashiorkor—there is a high incidence of ariboflavinosis in the adult population of Southern Nigeria the lesions of kwashiorkor are similar to those of ariboflavinosis and both have parakeratosis as the underlying epithelial histological process the mode of death in kwashiorkor may be sudden with coma, as in dogs suffering from ariboflavinosis SEBRELL [*Bulletin of Hygiene* 1930 v 5 374] has shown that deprivation of riboflavin in dogs may lead to fatty liver and death in coma. Riboflavin however will not bring about recovery in the late stages and Hughes suggests that deficiencies in other vitamins may be present

Deficiency of riboflavin may be prevented by the use of milk or yeast in the diet. Milk is expensive and in the tsetse belt of Africa may be impossible to obtain but food yeast at a cost of less than a farthing a day would prevent the condition

Charles Wilscocks

REINGOLD I M & WEBB F R Sudden Death following Intravenous Injection of Thiamine Hydrochloride *J Amer Med Ass* 1946 Feb 23 v 130 No 8 491-2. [13 refs]

1 Sudden death followed an intravenous injection of a solution of thiamine hydrochloride.

2 The patient had been given four injections at frequent intervals prior to death. Following the last injection she complained of a generalized burning perspired profusely became dyspnoeic and cyanotic and soon died.

3 The death is considered an example of an anaphylactic shock, the thiamine hydrochloride being the anaphylactogen

4 Pathologically the anaphylaxis probably manifested itself in constriction of the smooth muscles of the pulmonary arteries and bronchioles resulting in pulmonary engorgement and right heart dilatation and failure and in mild pulmonary emphysema respectively In addition small foci of polymorphonuclear leukocytes and round cells were seen in thickened septums of pulmonary alveoli. Foci of pigmented macrophages probably indicated that previous hemorrhages had occurred following an anaphylactizing injection.

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## HAEMATOLOGY

MURPHY R C Jr & SHAPIRO S The Pathology of Sickle Cell Disease *Intern Med* 1945 Sept. v 23 No 3 376-97 6 figs. [42 refs.]

In sickle cell disease the sickling is an inherent property of the red cell and is determined by the ratio of oxyhaemoglobin to reduced haemoglobin within the cell. It appears that each cell has a specific threshold or level of haemoglobin in the reduced form at which it will sickle. Once this threshold is



to hospital. He complained of pain on swallowing but there was no dyspnoea, no headache vomiting or diarrhoea. Prior to admission he had been given  $\frac{1}{2}$  grain morphine sulphate 500 cc. of whole blood and 1 000 cc. of saline intravenously (also for some unexplained reason 2 gm. sodii bicarb. per os every 4 hours). When he was admitted the site of the bite was anaesthetic and his speech was "thickened" from swelling of the lips face and tongue. The face scalp and neck were brawny with non-pitting swelling there was no respiratory obstruction, no nervous symptoms were present and the reflexes were normal. Blood examination gave red cells 3,240 000 and white cells 8 000 per cmm (87 per cent. polymorphonuclears). Ten cc. (one unit) of Brazilian antivenene was given intramuscularly 9 $\frac{1}{2}$  hours after reception of the injury. [Nothing is said of the constitution of this antivenene but the statement is made that it was known not to be specific for the venom of this snake.] In another 8 $\frac{1}{2}$  hours the oedema had involved the right shoulder and upper part of the chest in front and there was some dyspnoea from swelling of the tissues. Fourteen hours later still, i.e. 32 hours after the bite the swelling had spread all over the front of the chest being more marked on the right side. The patient was coughing up some mucopurulent sputum. Penicillin was started [dose not stated] to guard against secondary infection. In two days there was no further swelling nor any more dyspnoea but the swelling had become ecchymotic. The pulse-rate had kept about normal 70-80 per minute and the blood pressure unaltered. On the fourth day the skin over the swollen area was purple to blue-black. Another blood count gave leucocytes 4 600 per cmm., with differential percentages normal. During the succeeding week the swelling gradually subsided, and a fortnight after his admission the patient returned to duty the only residual symptom being slight swelling of the left cheek and upper eyelid.

Five of the eight patients received the Brazilian antivenene at intervals ranging from one to ten hours after infliction of the bite and the author remarks "such a small number of cases affords no true index of the value of the Brazilian antivenom" however it is the writer's opinion that those who received the antivenom late or not at all, recovered as well as those who received it early. [In view of the specificity of most snake antivenenes this is not surprising.]

H. Harold Scott

WYON P. H. Four Cases of Russell's Viper Bites. *Brit Med J* 1945  
Dec. 29 919-20 1 fig

Four cases of snake-bite incurred in Central Burma are described, one of which was fatal. The snakes responsible were identified as Russell's vipers apparently by the author. The identity of the largest which measured 4 ft. 6 in. was confirmed by the local district laboratory.

The routine treatment is described in detail. A tight tourniquet was applied to the limb above the bite and antivenene was at once given intravenously. The patient was anaesthetized with pentothal, and incisions were made "in the line of the bite" down to but not through the deep fascia unless the fascia had been penetrated by the bite. The cases were then treated by venesection from the affected limb and by retaining a venous tourniquet for as long as 18 hours. By releasing the tight tourniquet regularly intermittent venesection was achieved. Later the patient was transfused if necessary.

The author discusses certain clinical aspects of snakebite and its treatment. Most unfortunately no autopsy was carried out in the fatal case. This patient was given antivenene soon after being bitten on the right wrist and was

first seen by the surgeon about 8½ hours later. He died as far as can be made out from the case history about 29 hours after the bite.

B G Macgrath

## DERMATOLOGY AND FUNGUS DISEASES

MOURÃO B M O papel do estreptococo no pénfigo foliaceo (fogo selvagem)  
Estudo clinico-bacteriologico [The Part played by Streptococci in Pemphigus foliaceus (Wild Fire) Clinical and Bacteriological Study] Mem Inst Butantan 1943 v 17 141-285 28 figs. & 8 graphs [83 refs.]  
English summary

Though this monograph first saw the light nearly three years ago it may be regarded as up to date since no work has been done on the subject in the interval. It may be looked upon as a complete monograph on *pemphigus foliaceus* and its association and possible aetiological connexion with streptococci. It comprises more than this for it includes a brief review of the rôle of streptococci in dermatology.

The whole is divided into twelve chapters of which the first is introductory and the last two sum up the rest. The introductory chapter tells of the investigations of LINDENBURG on *pemphigus foliaceus* and Dühring's *dermatitis herpetiformis* and his conclusions that the former was an infective disease due to a virus which circulated in the blood and was transmissible to laboratory animals notably rabbits and guinea-pigs. Others however and the present author among them were unable to confirm this and took up the study afresh, this time from a bacteriological angle to investigate methodically the pyogenic bacteria in pemphigus and dermatoses generally, bullous or otherwise. The second chapter reviews previous published work on streptococci in dermatoses of the pemphigus group and concludes that the organisms are not important primarily but are ready secondary invaders of the bullae. Chapter III states the plan proposed, which includes skin culture, blood culture, bacterial study of material taken ante- and post mortem, identification of the types isolated, their toxins and their pathogenicity for laboratory animals. Chapter IV speaks of the material for study obtained from 160 cases of this disease including 87 of the generalized chronic form, 38 in the primary bullous stage, 15 of general dermatosis, the dystrophic form, 12 with localized dermatosis or *formes frustes*, 8 in the regressive stage and 2 healed cases, one with cutaneous sequelae and one without. In chapter V details of the results are given. Skin cultures were made from 55 patients among them 21 in the generalized chronic stage and 16 in the invasion stage, cultivations were tried from the bullae, from crusts and from fluid obtained by puncturing the bases of bullae. Of 53 cases (2 had recovered) 43 had streptococci in the lesions. Not in a single one of those in the primary bulla stage with clear fluid, were streptococci found, but in all those with purulent contents or those crusted over without exception. In the latter there might also be *Staph albus*, *Staph aureus*, *Bact coli* and diphtheroids. In the *formes frustes* streptococci were isolated from 25% the haemolytic form in 12.5% and inert streptococci in 12.5% [but only 8 cases of this form were examined by skin culture so these figures would imply that haemolytic streptococci were found in one case only and the same as regards non-haemolytic streptococci. To state this as 12.5 per cent of cases tends to mislead.]

Of four cases of Dühring's *dermatitis herpetiformis* two gave a growth of haemolytic streptococci, one of them associated with *Staph albus*, a third gave *Staph aureus* only. Chapter VI tells of the results of haemoculture. This was done in 150 cases and streptococci were grown from 19 (12.6 per cent.)

the parasite and blood culture may prove of value in diagnosis but it necessitates some delay. The cutaneous sensitivity test with "histoplasma" is as yet of undetermined diagnostic value. The prognosis is almost uniformly unfavourable.

J. T. Duncan.

NIÑO F. L. Granuloma paracoccidioidico. Estudio de una nueva observación en la República Argentina. (Nota previa) [Paracoccidioidal granuloma. Study of a New Case in the Argentine Republic. Preliminary Note.] *Rev Asoc Med Argentina* 1945 July 30 v 59 No. 562, 830-34 7 figs.

This is a report of a new case of paracoccidioidal granuloma in which the infection appears to have been contracted in Buenos Aires. The patient, a man aged 44 was a trader in charcoal and maize materials from which, the author considers the infecting fungus may have been derived. The lesions were situated in the mouth and there was an associated mass of enlarged and suppurating glands, the size of a pigeon's egg in the neck. The lungs were also involved and the parasite was found in the sputum and in material aspirated from the bronchi with the aid of the bronchoscope. The diagnosis was made by microscopical examination of the sputum, tissue obtained by biopsy and pus from lymphatic glands and was confirmed by cultivation of the fungus and by the results of the inoculation of morbid material into guinea-pigs.

J. T. Duncan

## TROPICAL OPHTHALMOLOGY

- i. DANSEY BROWNING G. C. & RICH, W. M. Ocular Signs in the Prisoner of War returned from the Far East. *Brit Med J* 1946 Jan. 5 20-21 [11 refs.]
- ii. RIDLEY H. Ocular Manifestations of Malnutrition in released Prisoners of War from Thailand. *Brit. J Ophthalmology* 1945 Dec. v 29 No. 12, 619-18.
- iii. GARLAND H. G. Ocular Signs in the Prisoner of War from the Far East. [Correspondence.] *Brit Med J* 1946 Jan. 26 143.
- iv. CHURCHILL, M. H. Dietary Deficiency Diseases among Prisoners of War. *J Roy Army Med Corps* 1945 Dec. v 85 No. 8 294-8.

i. The ocular signs of malnutrition in prisoners of war returned from the Far East are discussed by DANSEY BROWNING and RICH. They examined some 30 men who were released at the recapture of Rangoon, and who had been prisoners for 2 to 3 years. Ten subjects were found to have bilateral scotomata, with a 'tail' to the white scotoma leading from the fixation spot towards an enlarged blind spot. There did not appear to be any nuclei lying between the blind and fixation spots. There was no constancy in the colour scotomata. In not one of these 10 subjects was there contraction of the peripheral visual field either to white or to colours. All 10 showed some degree of visual failure and in five the corrected vision could not be brought above 6/60. The ophthalmological examination revealed that all 20 optic disks showed some degree of pallor. Four of the disks showed an apparent primary optic atrophy, four showed pallor of the papillomacular bundle, and eight showed pallor of the temporal half. No case showed ocular muscle paresis. No diminution of sensitivity of the cornea and conjunctiva was found, neither was there any evidence of xerosis nor any of the ocular signs of anisochlorosis.

The authors consider that there is a relationship between the scotomata to white and those of the toxic amblyopias and that the deficiencies of vitamins B<sub>1</sub>, B<sub>2</sub> and (very dubiously) A appear to play their part in the ocular signs of beriberi although the exact nature of the deficiency remains obscure. They conclude that as the optic nerve is part and parcel of the c.n.s. the damage done to the nerve proper by the axial optic neuritis of beriberi is final, and that any improvement of vision can be but slight.

ii. The ocular manifestations of malnutrition in some 500 released Allied prisoners-of-war and internees from Thailand who considered that their sight had deteriorated during captivity are discussed by RIDLEY. Among these no fewer than 100 cases of amblyopia were seen in 17 days and many of those whose corrected vision was normal had subclinical vascular lesions of the eyes. Visual failure occurred in 90 of these patients between October 1942 and December 1943 so that their sight had been defective for 2½ to 3 years. Acuity with correction varied between 1/60 and a partial 6/6 nine read less than 6/60 with the better eye sixteen 6/60 twenty six, 6/36 fifteen 6/24 fifteen 6/18 seven 6/12 eight 6/9 and four 6/6. All those with scotomata and good acuity reported recovery from temporary severe amblyopia. In many cases the onset had been sudden maximum disability being reached within a single day though in others it was gradual taking months to develop. There was some degree of photophobia and sight was particularly defective in bright light but few of the subjects complained of difficulty in seeing at night. Many patients with amblyopia gave histories indicating that in addition to recurrent attacks of the common tropical infections they had suffered from pellagra, oedema of the lower extremities dry beriberi, and from sore tongue and *perlèche* which usually accompany deficiency in the B group of vitamins. A high proportion of the cases had become nerve deaf. In the fundus there may be no visible abnormalities even when the amblyopia is severe and of long standing though in many of the severe cases there is definite pathological pallor of the temporal half of the optic disk the colour becoming grey rather than pure white. There were 48 cases of optic atrophy and 30 more were regarded as doubtful in this respect. Nothing was ever found that was suggestive of past oedema of the nerve head the retinal vessels were not constricted and the macular area and its surrounding vessels generally appeared normal though in a few instances in which temporal pallor was marked there appeared to be some reduction in the calibre of the macular arterioles a change probably secondary to retinal atrophy.

Campimetry revealed in 90 cases a small sharply-demarcated central scotoma rarely extending more than 3° and sometimes only 1° from fixation and often less though within this area in severe cases even a 40-mm white object was invisible at 1 metre. The edges of this scotoma are abrupt its density rather than its size being the important variable. In the remaining 10 cases the core of the scotoma was para- or peri-central and situated within the 3° circle the fixation area showing less visual depression. In this type the affected area was usually more extensive and the peripheral margin especially was less abrupt and extended as far as the 5° circle. In four of these cases the scotoma appeared to be limited by the horizontal meridian on both sides of the fixation point. Some patients with this type of field say that some portion of a letter or some letters in a line are invisible and that objects tend to appear and disappear. In the majority of these cases there was a history of considerable improvement during captivity which is in accordance with the shelving edge of the scotoma.

No defects were discovered in the peripheral fields.

Practically all the released prisoners showed some degree of keratoconjunctival abnormality. There was no gross injection, except occasionally in the interpalpebral area where the conjunctiva might be dull thickened or opaque. No

xerosis nor Bitot's spots were seen. In 86 per cent. of the amblyopic and 91 per cent. of the other patients the fine capillary plexus at the limbus was increased in extent and minute superficial vessels extended as far as 2 mm. into the cornea. The vascularization was accompanied by superficial opacification. Frequently the internal margins of capillary loops united to form quite large circumferential vessels. The most striking feature of the limbal capillaries was their variability in size which was often so great that aneurysms both fusiform and saccular appeared. These were situated rather more frequently on the scleral than on the corneal portion. Aneurysms were present in 65 per cent. of the scotomatous patients and in 43 per cent. of those with normal sight. No haemorrhages were observed. There seems little doubt that the lesions described are *due primarily to malnutrition though there may be other factors since only a small proportion of men living under identical conditions were affected*. There is no doubt that the diet was deficient generally especially in protein and fats as well as vitamins and, in the absence of direct evidence that avitaminosis unsupported by other factors is the cause it seems advisable to attribute the lesions to general malnutrition rather than simple deficiency of the B group. The abnormal vascularity of the limbus suggests a deficiency of vitamin B<sub>2</sub>, although healthy soldiers who have been in a tropical climate for some time have some increase in the limbal plexus.

It is uncertain whether the disturbance in the visual pathway originates in the retina or the optic nerve nor is the mechanism whereby the neurones are affected understood. In view of the known abnormality of the conjunctival capillaries it is tempting to postulate a vascular origin—failure of the choriocapillaris to nourish the outer layers at the macula or if the limitation of some fields by the horizontal meridian has any significance failure of the macular branches of the superior or inferior divisions of the central artery to nourish the inner layers of the retina. There is however no concrete evidence to support such a theory.

iii GARLAND in discussing the ocular signs in the prisoner-of-war from the Far East considers these to be a constant feature in an interesting syndrome there is also commonly bilateral nerve deafness of a varying degree with a spinal cord syndrome. The latter is usually a picture of posterior column dysfunction (but occasionally with pyramidal signs) the legs being affected more than the arms. In some cases the syndrome has been further complicated by intellectual deterioration. That this syndrome is due to a dietary deficiency seems almost certain but it seems equally certain that it has nothing whatever to do with vitamin B<sub>1</sub>. It is very doubtful whether it has anything to do with vitamin B<sub>2</sub> and certainly in some of the cases the syndrome has existed throughout its course with no evidence of beriberi or pellagra. At the same time scrutiny of the diet on which the picture develops suggests that the deficiency is probably in the B group of vitamins though a deficiency of vitamin A has not yet been excluded. Garland has little doubt that some of these subjects did in fact suffer from beriberi but he suggests that the beriberi was a co-existing deficiency picture he considers that the lesion underlying the visual failure lies in the optic nerve but he does not describe it by the term 'retrobulbar neuritis' as there is no proof that it is an inflammatory condition.

iv Ophthalmic abnormalities occurring among nearly 800 cases of deficiency disease in prisoners-of-war in Singapore and Thailand during 1942 to 1945 are discussed by CHURCHILL. Avitaminous amblyopia (neurorretinitis) was a common condition, the first cases appearing within four months of the prisoners going on to the Japanese ration scale. In August, 1945 in one camp in Thailand, 81 men out of 1,200 were affected but a considerable number of men suffering from this condition had already died from other diseases. Of these 81 cases, 10 followed shortly on an attack of dysentery in 16 there was an association with

beriberi in 4 with stomatitis in 3 with happy feet (nicotinic acid deficiency) and in 2 with pellagra. The outstanding symptom was a blurring vision but this was preceded by a smarting of the eyes lachrymation and photophobia. When working in the sunlight many of the patients experienced actual pain behind the eyes. The blurring was first noticed on reading but soon some of the men were unable to recognize people or objects out-of-doors. The failure of sight was often progressive and severe in other cases it progressed to a certain extent and then remained stationary in others again it improved when there was any substantial improvement in the diet. These men had subjective scotomata but rough tests revealed no impairment of the visual fields. Ophthalmological examination showed a retina which was often redder than normal with swollen veins. The disk was pink and its margins were frequently blurred occasionally the temporal half of the disk was quite white. Among 72 cases some degree of cupping or excavation of the disk was present in 36 and the lamina cribrosa was seen in 8. A puzzling feature of this disease was the apparent lack of correlation between the visual defect and the extent of the ophthalmoscopic changes.

Night blindness was a rare condition among the prisoners-of-war occurring in only 3 out of 1,200 men. It was associated with only 1 of the 81 cases of avitaminosis amblyopia. This comparative rarity was probably due to the fact that pumpkins rich in carotene were a fairly constant item in the ration scale. Four out of some 1,200 men suffered from corneal ulceration and this was not more common among the prisoners than amongst British troops in the tropics.

E O G KIRWAN

## HEAT STROKE AND ALLIED CONDITIONS

1. SPECTOR H MITCHELL H. H & HAMILTON T S The Effect of Environmental Temperature and Potassium Iodide Supplementation on the Excretion of Iodine by Normal Human Subjects *J Biol Chem* 1945 Nov v 161 No 1 137-43
11. — HAMILTON T S & MITCHELL, H. H The Effect of Pantothenic Acid Dosage and Environmental Temperature and Humidity upon the Dermal and Renal Excretion of Pantothenic Acid. *Ibid* 145-52. [15 refs.]
111. SHIELDS J B JOHNSON B C. HAMILTON T S & MITCHELL H H. The Excretion of Ascorbic Acid and Dehydroascorbic Acid in Sweat and Urine under different Environmental Conditions. *Ibid* 351-8.
- 1V JOHNSON B C MITCHELL, H H & HAMILTON T S The Occurrence of Inositol and of *p*-Aminobenzoic Acid in Sweat. *Ibid* 357-60

These papers are based on results obtained during a 2-year study of the effects of high environmental temperature and variable humidity upon the dermal losses of certain minerals and vitamins and their metabolites. Five men aged from 20 to 28 years spent eight hours a day in an air-conditioned room five days a week. The conditions were alternate weeks comfortable (86°F 50 per cent. relative humidity) and hot moist (100°F 69 per cent. relative humidity). Other conditions were sometimes imposed. The subjects were apparently at rest. Sweat losses calculated in the usual way were for comfortable conditions 80 gm per hour and for hot moist conditions 670 gm per hour (averages from pooled results of the four papers). There is one inconsistency in that in the second paper subject C is shown as sweating

[June, 1946]

at 79 gm. per hour in week 28 and in the fourth paper at 27 gm. per hour this is not a misprint, as the averages for the group are correspondingly different). The loss during comfortable conditions though high, was attributed by the author to insensible perspiration [true insensible perspiration rarely exceeds 40 gm. per hour]. The mean sweat loss in hot-moist conditions varied between 40 gm. per hour and 814 gm. per hour for different weeks. There was no regular variation attributable to acclimatization. Sweat (i.e. pooled skin excretions) was collected on waterproof sheets and on swabs and was added to distilled water washings from the body clothes and towels to form for each subject each day a single bulk specimen for analysis containing all the skin excretions for that day. On Saturday mornings undiluted sweat was collected under hot moist conditions by collecting the drips off the subjects as they stood in pans (no allowance was made for evaporation though some probably occurred). Faeces and urine were also collected and analysed.

i. *Iodine excretion*—The loss of iodine in the insensible perspiration was 2.5γ per 100 cc. when no iodine supplement was being taken but in frank sweat (undiluted samples) it was only 0.85γ per 100 cc. The total skin loss was however greater when sweating 6.1γ per hour compared with 2.2γ per hour. A supplement of 2 mgm. potassium iodide per day did not affect the iodine losses in the insensible perspiration but increased the losses in sweat from 0.85 to 3.65γ per 100 cc. (undiluted sweat) and from 1.5 to 17.7γ per hour. The urinary loss was in all cases more than 75 per cent. of the total excretion but it was slightly less in hot moist conditions, than in comfortable conditions when an iodine supplement was given thus balancing the increased skin loss. Faecal excretion after extra iodine was greater in hot moist than in comfortable conditions but it was the same under both conditions without the supplement.

ii. *Pantothenic acid excretion*—About 8γ of pantothenic acid were lost per 100 gm. insensible perspiration. Undiluted sweat contained 3.8γ per 100 cc. increasing the relative humidity did not significantly increase the concentration. Losses of pantothenic acid per hour from the skin were about 8γ under comfortable and 25γ under hot moist conditions. Supplements of up to 18 mgm. calcium pantothenate per day did not increase the concentration in either insensible or sensible perspiration. Urinary excretion of pantothenic acid was slightly greater under hot moist conditions but the proportion of the total excretion found in the urine fell from 97.6 per cent. to 87.3 per cent. owing to the very much greater rate of excretion via the skin. Thirty-one per cent. of an 18 mgm. dose of calcium pantothenate was recovered from the urine. The authors discuss their results in relation to the fact that they used results by other workers and attribute differences to the fact that they used *Lactobacillus arabinosus* as test organism whereas others had used *Lactobacillus casei* which may be stimulated by fatty materials in the sweat.

iii. *Ascorbic acid excretion*—No rubber equipment was used in the study as it has repeatedly been shown that sweat which has been in contact with rubber reduces 2, 6-dichlorophenol-indophenol and hence has an apparent ascorbic acid content whereas sweat collected in 82 samples of sweat were found to contain ascorbic acid but by the 2, 6-dinitrophenyl-hydrazine procedure of Roe and another free ascorbic acid was found in five out of eight specimens tested, in a mean concentration of 33γ per 100 cc. By the same method an average of 70γ of dehydroascorbic acid was found per 100 cc. of sweat. In one experiment daily doses of 500 mgm. of ascorbic acid decreased the ascorbic acid content of the sweat from 33γ per 100 cc. in the control week to 5γ while the dehydroascorbic acid content increased from 34γ to 107γ per 100 cc. In another period and with the same daily doses the dehydroascorbic acid content was only 68.5γ per 100 cc. The combined skin losses of ascorbic

and dehydroascorbic acids were equivalent to 2.74 mgm only per day even with profuse sweating hence skin losses do not noticeably affect vitamin C requirements. Urinary losses of ascorbic acid were greater at high humidities than under comfortable or hot-dry conditions.

*Inositol and p-aminobenzoic acid excretion*—The concentration of inositol in sweat was found to be 21% per 100 cc. under hot moist conditions the loss per hour was 0.118 mgm. compared with a loss of 0.027 mgm under comfortable conditions. Urinary excretion was variable. The average concentration of p-aminobenzoic acid in sweat was 0.24% per 100 cc.

W S S Ladell

BURCH G E The Influence of Environmental Temperature and Relative Humidity on the Rate of Water Loss through the Skin in Congestive Heart Failure in a Subtropical Climate. *Amer J Med Sci* 1946 Feb v 211 No 2 181-8 4 figs [11 refs]

Water losses were measured from three small areas of skin first in a comfortable atmosphere (dry bulb 70°F wet bulb 62°F relative humidity 60 per cent) and then in a hot humid atmosphere (dry bulb 104°F wet bulb 83°F relative humidity 64 per cent). The areas chosen were the tip of the index finger on the shin and on the volar surface of the forearm all on the right side. The measurements were made by directing a stream of dry oxygen over the skin and then condensing the water taken up the amount recovered being estimated gravimetrically. Five groups of subjects were tested (a) eleven normal subjects (b) ten patients with diseases other than congestive heart failure (c) five patients with slight to moderate failure (d) five patients with moderate to severe failure (e) ten patients with severe failure. Under comfortable conditions the losses were the same in all groups with finger losses about 50 per cent greater than skin and forearm losses. In hot humid conditions finger losses showed a 4-fold increase and the other losses more than an 8-fold increase (compared with the losses under comfortable conditions) in the normal, non heart failure and slight heart failure groups but in the moderate and severe heart failure groups finger losses increased only 2.5 times for both groups and the other losses 4 times and 2.5 times respectively. Thus local sweating in these two groups was impaired relative to the rest.

This impairment of local sweating is Burch considers a manifestation of congestive heart failure [he is no doubt correct but he weakens his case by drawing his main conclusions from the comparison between a control group average age 26 comprising nine white men one white woman and one coloured woman and a severe heart failure group average age 54 comprising four coloured women three coloured men and one white man]. Diminished local sweating indicates Burch argues a generalized and marked impairment of the emergency sweating mechanism predisposing to the accumulation of body heat. [He would be on surer ground if he had taken measurements from more areas see WEINER, this *Bulletin* 1946 v 43 249 no measure-ments are given of the body temperatures in any of the subjects though reference is made to observations by other authors on pyrexia in patients with congestive heart failure in comfortable environments.] The ability to sweat Burch states returns with recovery of the cardiac function but no serial observations on a patient during recovery are given in support of this. In his discussion the author emphasizes the importance of cool comfortable conditions for patients with congestive heart failure in order to keep the demand on the cardiovascular system as low as possible and he therefore recommends air-conditioned wards especially in warmer climates.

W S S Ladell



## Tropical Diseases Bulletin.

Koch W. Three Rapid Tests for the Estimation of Tropical Fitness of Fabrics. *J Hygiene* 1946 Jan. v 44 No. 4 288-8, 3 figs.

The author suggests that the fabric for use in the tropics may be decided by considerations of its thermal insulation quality and its air porosity only. After describing how an estimate of insulating power can be obtained by comparing the cooling rate of a kata thermometer clothed with the fabric with the cooling rate when it is uncovered, this author discards this in favour of a simple measurement of thickness. REES (*J Textile Inst* 1941 v 32 T 149) showed that thermal insulation, measured in the laboratory is among other things a function of the thickness of the fabric. Koch accepts this as applicable to physiological conditions, and describes a simple optical method of measuring thickness. Instead of measuring air porosity, he suggests that the stretched layer of the fabric should be determined. He found a correlation of  $-0.78$  between the two values when plotted fall accurately on a rectangular hyperbola and are probably therefore not his original experimental data. [Physical considerations would in any case suggest the hyperbolic relationship; (The author completely ignores other physical properties of fabrics such as water vapour permeability and water absorbing power)] W S S Ladd.

BAXTER, S. Heat and Water Vapour Transfer through Fabrics. *J Textile Inst.* 1946 Mar v 37 No 3 T32-57 15 figs. [11 refs]

## MISCELLANEOUS DISEASES

CHALGREN W S & BAKER A B. Tropical Diseases. Involvement of the Nervous System. *Arch Pathology* 1946 Jan v 41 No 1 68-117 [305 refs]

BRIXTON D. An Unusual Form of Epidemic Food-Poisoning with Neurological Symptoms. *Proc Roy Soc. Med* 1948 Feb v 30 No 4 173-5 (Sect. of Neurology 5-7)

During 13 months October 1942—November 1943 some 450 persons in Aden had suffered from *wiswara* poisoning from eating imported wheat contaminated by the weed flax-darnel or *Lolium temulentum*. The local word *wiswara* is said by the author to mean tipsy and the symptoms are very characteristic of this state: dizziness, headache, tremors, lassitude, slurred speech and staggering gait. Sometimes gastro-intestinal disturbance. If much has been taken the patient may become comatose for several hours. No deaths were reported. The condition recorded and the fact that in ordinary circumstances Abyssinian wheat are rare is due to the care with which the weed is separated from the wheat.

The actual toxic element is said to be some pyridine base in the mould seen on nearly every weed-seed. [This form of poisoning has been known in India for many years. Concerning it the reviewer wrote in 1920 "Lolium temulentum bearded darnel, known as mostaki (Punjab) and moschni (N. W. Provinces). Bread made with flour partly constituted by the seeds of this plant sets up the following symptoms: vertigo, staggering gait, nausea, vomiting, dim vision (perhaps green), tremors of arms, legs and tongue with dysarthria, a burning pain in the mouth and throat, and general prostration with a weak, irregular

pulse. No fatal cases have been reported. It is not known whether the poisoning may not be due to an associated symbiotic fungus. *The Practice of Medicine in the Tropics* Byam & Archibald 1921 v 1 782.] *H Harold Scott*

COHEN S C EMERT J T & Goss C C Poisoning by Barracuda like Fish in the Marianas. *U S Nav Med Bull* 1946 Feb v 46 No 2 311-17 2 figs

Two outbreaks of food poisoning are recorded in the same district one affecting 41 persons of an officers mess in a Military Government camp on Saipan the other affecting 10 civilians (Koreans) in an internee camp on Saipan. The poisoning is ascribed to eating barracuda like fish from which it would be inferred that the actual diagnosis was not made but the article is illustrated by drawings of *Sphyræna barracuda* and *Ruvettius pretiosus* (oil fish).

The fish eaten in the officers mess was a large one 55 lb and was eaten 27 hours after being caught at the internee camp the 10 poisoned were among 30 who partook of it 8 hours after it had been caught. Both fish had been caught at the same time and at the same place.

The symptoms were typical. About 4 hours after eating the fish there set in severe muscular spasms of the limbs with cold clammy extremities paresis of the muscles of deglutition dyspnoea apnoea burning sensations in the mouth and tongue and cutaneous hyperaesthesia so that cold drinks and cold baths could not be taken. There was in most a certain degree of shock. Just a year previously in the same Journal Feb 1945 a closely similar outbreak due to the same cause and in the same area was reported [see this *Bulletin* 1945 v 42 592 where a fairly full comment is given] *H Harold Scott*

MENON I G K Intestinal Fusio-Spirochaetosis. *Indian Med Gaz* 1945 Sept v 80 No 9 454-8 7 figs on 1 pl.

The author found fusiform bacilli (*Fusiformis fusiformis*) and spirochaetes (*Treponema vincenti*) in the faeces of 16 out of 120 persons examined. Notes of clinical and laboratory findings and of treatment are given in the case of four of them and the other twelve are tabulated under the headings clinical condition cellular exudate other infections and spirochaetes. In the four cases described there were sudden attacks of abdominal pain above the umbilicus and of diarrhoea lasting for a day or two or sometimes for a few weeks. Duodenal intubation was done in one patient and spirochaetes and fusiform bacilli were found in the fluid withdrawn. These organisms were present on the gums of all four patients. Of the other 12 patients 4 had amoebic dysentery and 2 had a history of amoebic infection 2 had pain and diarrhoea one had chronic dyspepsia 1 had upper abdominal pain and 2 had no symptoms. *Giardia intestinalis* was present in 6. Treatment with stovarsol appeared to cure the symptoms. The possibility that the fusiform bacilli and spirochaetes may cause the symptoms with which they are associated is discussed with references to the work of other authors. *J F Corson*

TOULLEC, F La mélioidose. [Meloidosis.] *Les Grandes Endémies Tropicales* (Onzième Année) 1939 Paris pp 49-59

WEBB A C Primary Carcinoma of the Liver *Arch Pathology* 1945 Nov-Dec v 40 No 5 382-6 9 figs [27 refs.]

A survey of the literature shows that primary carcinoma of the liver is comparatively rare in this country [the United States] and in Europe. The incidence is much higher among some groups of Orientals and Africans.

KOCH W. Three Rapid Tests for the Estimation of Tropical Fitness of Fabrics. *J Hygiene* 1946 Jan., v 44 No. 4 2S8-8 3 figs.

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[The author completely ignores other physical properties of fabrics such as water vapour permeability and water absorbing power.] W S S Laddell

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During 13 months October 1942—November 1943 some 450 persons in Aden had suffered from *wiscara* poisoning from eating imported wheat contaminated by the weed flax-darnel, or *Lolium temulentum*. The local word *wiscara* is said by the author to mean *tipav* and the symptoms are very characteristic of this state: dizziness, headache, tremors, lassitude, slurred speech and staggering gait, sometimes gastro-intestinal disturbance. If much has been taken the patient may become comatose for several hours. No deaths were reported. The condition recorded and the risks from eating contaminated Abyssinian wheat are well known and the fact that in ordinary circumstances cases of poisoning are rare is due to the care with which the weed is separated from the wheat.

The actual toxic element is said to be some pyridine base in the mould seen on nearly every weed-seed. [This form of poisoning has been known in India for many years. Concerning it the reviewer wrote in 1920: "*Lolium temulentum* bearded darnel, known as mostaki (Punjab) and moschini (N W Provinces). Bread made with flour partly constituted by the seeds of this plant sets up the following symptoms: vertigo, staggering gait, nausea, vomiting, dim vision (perhaps green), tremors of arms, legs and tongue with dysarthria, a burning pain in the mouth and throat, and general prostration with a weak, irreg-

BAYLEY E C LINDBERG D O N & BAGGENSTOSS A H Loeffler's 81  
Report of a Case with Pathologic Examination of the Lungs. *Arch P*  
1945 Nov-Dec. v 40 No 5 376-81 5 figs. [Refs in footnotes]

KATTENELLENBOGEN I Behcet's Triple Syndrome. (Report of Three Cases)  
*Harefuah*. Jerusalem. 1946 Feb 15 v 30 No 4 [In Hebrew 81-4 (19 refs.)  
English summary 84]

See also this *Bulletin* 1944 v 41 780

BOLAND E W HEADLEY N E. & HENCH P S The Treatment of Agranulo-  
cytosis with Penicillin. *J Amer Med Ass* 1946 Mar 2, v 130 No 9  
556-9, 1 fig [Refs. in footnotes.]

Since 1941 sulfonamides and penicillin have been used in the treatment of granulocytopenia or agranulocytosis. At first they were used more often despite the presence of agranulocytosis rather than specifically for it. Seven cases of agranulocytosis successfully treated with sulfonamides have been reported. But because sulfonamides may themselves produce agranulocytosis penicillin would seem to be the remedy of choice.

Ten cases of agranulocytosis including the one here reported have now been treated with penicillin prompt recovery has occurred in every case. This represents a notable improvement in the treatment of the condition and allows for much greater optimism in prognosis than has heretofore been possible. In some of these 10 cases leukopoietic agents were used in conjunction with penicillin but the current trend is to rely on penicillin alone. Experiences to date indicate that penicillin constitutes the most potent remedy at hand for the prevention or control of the serious potentially fatal complication of agranulocytosis.

Since this paper was submitted for publication another case of agranulocytosis successfully treated by penicillin has been reported. Thiouracil had been given for hyperthyroidism the leukocyte count fell to 2 400 with 2 band cells and 2 segmented neutrophils. Treatment included a transfusion liver extract and a total dose of 560 000 units of penicillin in four days after which recovery was complete.

KEAN B H TUCKER, H. A & MILLER W C Ainhum: a Clinical Summary  
of Forty-Five Cases on the Isthmus of Panama. *Trans Roy Soc Trop*  
*Med & Hyg* 1946 Feb v 39 No 4 331-4

In the 40 years ending May 1944 45 cases of ainhum have been traced in Panama this number represents 1.5 per 10 000 West Indian male admissions to hospital. All the ainhum patients were West Indians 20 from Jamaica 10 from Barbados they were all males and none was white or half-caste. Thirteen were between 21 and 30 years of age at the onset of the disease 11 between 41 and 50 8 between 31 and 40 Six had the condition before coming to Panama and in two-thirds of the cases just over 11 years elapsed between arrival in the district and onset of symptoms. The little toes were involved in all both sides in 14 the right alone in 18 the left alone in thirteen. In one patient the third and fourth toes were affected, also on both sides. In one only was there a family history the father having been similarly afflicted.

Pain was marked, in fact the chief symptom for which hospital relief was sought. A history of local trauma was elicited in 4 only. No evidence was obtained of any aetiological connexion between ainhum and leprosy, syphilis, scleroderma or arteriosclerosis and the author postulates hereditary racial tendency as the main factor [which if it has any meaning at all is purely hypothetical.]

H Harold Scott

"To a total of 1,200 cases in the literature 12 cases are added. All the patients were American Negroes. The incidence is seen to be higher in Negroes than in the general population. The data on these additional cases include age and sex of patient type of tumour nodularity presence or absence of cirrhosis necrosis hemorrhage and extrahepatic metastases weight of the liver when available.

In the genesis of the disease the role played by cirrhosis is important.

Experimental carcinogenesis suggests dietary deficiencies acting as predisposing factors in explanation of the peculiar racial and geographic distribution of the disease.

TAYLOR C. E. The Racial Distribution of Nephritis and Hypertension in Panama. *Amer J Path.* 1945 Nov v 21 No 6 1031-4 1 fig [37 refs]

[Renal disease is one of the most obscure in human pathology and this article forms an interesting pathological study but leaves the question little if at all less obscure.]

For some years it has been known that racial groups living in Panama in close contact and under similar conditions show marked differences in the incidence of hypertension. Thus it is some seven times as common in the West Indians as in native Panamanians and in the younger age-groups the proportion might be as high as 16 to 1 as gauged by examination of more than 1,300 persons applying for employment. African negroes under natural i.e. primitive conditions generally have a relatively low blood-pressure and it is suggested that an important factor in causing the hypertension is adjustment to a new civilization and a new environment. [This by itself, is of course pure hypothesis.] The author has studied autopsy records for renal changes among 498 cases: 268 West Indian negroes 77 Panamanians 135 whites, and 20 miscellaneous. He presents by way of preliminary a table of histological criteria, dividing the renal changes into three main groups: glomerulo-nephritis (acute subacute or chronic) pyelo-nephritis (acute active chronic and healed) and nephrosclerosis (arterial and arteriolar) a fourth group in which the other three may be combined he designates "unclassified".

Generally in the whole number of 498 pyelo-nephritis was the most common nephrosclerosis fairly common glomerulo-nephritis relatively rare. The numbers in the races examined are so unequal that comparison except on general lines is of little value and as given in percentages the findings are apt to mislead or convey a wrong impression. But broadly speaking differences were striking. Thus among the West Indians half (49.3 per cent.) had some form of nephritis more than three times relatively as frequent (15.6 per cent.) as among the Panamanians among the whites it was 20.7 per cent. Pyelo-nephritis was twice as frequent in the West Indians as in the other races the arteriolar form of nephrosclerosis was more than seven times as common in the West Indians as among the Panamanians and three times as common as in the whites. Blood pressure readings were of the same order: West Indians 176/104 whites 159/88 Panamanians 136/89. Sex seemed to play no part in the distribution of renal disease and it is noted that "five per cent. of the negroes and whites had mild hypertension with no evidence of nephritis". The author suggests as an interpretation of this that "essential hypertension may occur in the whites and the West Indians whereas when hypertension develops in a Panamanian it is probably secondary to renal mischief."

H. Harold Scott.

BAYLEY E C, LINDBERG D O N & BAGGENSTOSS A H Loeffler's 8;  
Report of a Case with Pathologic Examination of the Lungs. *Arch P*  
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H Harold Scott

TYE, M. Ainhum. *New England J of Med* 1946 Jan 31 v 234 No 5 152-4 2 figs. [24 refs.]

"The first case from New England of ainhum, or spontaneous dactylolysis is reported. The results of pathological study and the roentgenologic findings are reported, and the literature is reviewed.

## GENERAL ENTOMOLOGY

DETHIER V. G. The Transport of Insects in Aircraft. *J Economic Entom.* 1945 Oct v 38 No 5 523-31

From December 1943 to April 1945 818 collections of insects were made in aircraft flying between India and the west coast of Africa. The author groups the 2,006 insects collected into 86 families and 13 orders. The order Diptera constituted 88.5 per cent of the total catch, and one species *Musca sorbens* accounted for 45.9 per cent. of all insects caught. Only ten mosquitoes were taken, owing to precautions observed at the airfields. There were some *Simulium griseicollis* between December and February in the Sudan, but no *Phlebotomus* during the sandfly season March to September.

The insects gain entry to the cabin when the aircraft is grounded. They either fly in or are carried in on passengers or cargo. There is no evidence that they enter during flight of the aircraft. No insects were found in the engine nacelles and the only species taken from dismantled or wrecked wing and tail spaces was *Musca sorbens*.

One hundred tests were made with caged *Anopheles gambiae* placed in the nacelles for flights ranging from fifteen minutes to four hours duration. In 99 instances all mosquitoes were dead after the flight and in one test they were so battered that they died soon after removal. Other tests showed that insects in the nacelles were killed during the take-off.

The author concludes that effective precautions taken on air fields reduced the number of insects entering the aircraft and that along the route studied insect control in the aircraft themselves is necessary in the cabins only.

H. S. Leston

BEAMENT J. W. L. Waterproofing Mechanism of an Insect Egg. [Correspondence.] *Nature*. 1946 Mar 23, 370

WEBB J. E. The Penetration of Derris through the Spiracles and Cuticle of *Ulophagus orinus* L. *Bull Entom Res* 1945 July v 36 Pt. 1 15-22 1 fig. 18 refs.

In *Ulophagus orinus* derris dust is shown to be absorbed through the spiracles and tracheal system. The amount of dust entering the tracheae is governed by the structure of the inspiratory spiracles and the rate of flow of the inspired air.

"Factors stimulating the rate of respiration of the insect—i.e. increased muscular activity, the presence of 5 per cent. carbon dioxide and a rise in temperature increase the rate of entry of derris into the body.

"Penetration of derris takes place slowly through the external cuticle at 30°C., but not at all at 20°C. It is postulated that the entry of derris through the cuticle probably depends on the hardness of the lipoid layer.

WEBB, J. E. & GREEN R. A. On the Penetration of Insecticides through the Insect Cuticle. *J Exper Biol* 1945 Dec v 22, Nos. 1/2, 8-20 2 figs.

Some previous observations showed that certain insecticides, e.g. Derris were more effective in the presence of solvents such as high boiling tar acids.

Since it seemed likely that the solvents acted by facilitating penetration an investigation into this possibility was undertaken.

Diphenylamine was chosen as the insecticide since it is soluble in a wide variety of organic solvents. It was first mixed with kaolin and 1 per cent by weight of the solvent was then added.

The sheep ked *Melophagus ovinus* was used as the test insect. Groups of five keds in corked specimen tubes received liberal doses of insecticide and were later examined for cessation of heart beat. In a previous paper by Wehb [above] it was shown that derms dust entered the spiracles in the present instance however such entry is negligible and the diphenylamine acts after absorption through the cuticle.

It was found that only certain solvents of diphenylamine increased the rate of action e.g. cresols, benzyl alcohol and 4-methyl-cyclohexanol. Other solvents for example carbitol and methyl benzoate did not produce this effect. The capacity of a solvent to induce rapid action is described as its carrier efficiency.

It is suggested that the cuticle covering an insect may be thought of simply as a two phase system comprising an outer phase of lipophilic elements associated with the epicuticle and an inner phase of hydrophilic elements associated with the exocuticle and endocuticle which is traversed by lipophilic elements. If this concept of the cuticle structure is accepted it can be seen that in order to reach the hypodermal cells below the cuticle the penetrating substance must traverse first a lipophilic and then a hydrophilic layer. Measurements were made of the rate of passage of solvents through beeswax (taken to represent the lipophilic layer) the solubility of the solvents in water, the partition coefficients of the solvents between beeswax and water, the solubility of the diphenylamine in aqueous solutions of the solvents and the volatility of the solvents. It was concluded that a high carrier efficiency could be correlated with a high rate of penetration through beeswax, a high partition coefficient of the solvent between beeswax and water and a high solubility of insecticide in a solution of the solvent in water. The volatility of the solvent and the solubility of the insecticide in it were also relevant factors.

As a result of the above observations it is suggested that solvents which facilitate penetration do so by transporting the insecticide across the lipid elements of the epicuticle to the interface between this layer and the water of the exocuticle. They also concentrate the insecticide in the epicuticle/exocuticle interface and so by raising the concentration there increase the diffusion gradient. Finally the solvents diffuse into the exo- and endocuticle and raise the partition coefficient between the solvent in the epicuticle and the water in the exocuticle.

Mixtures of two solvents each deficient in some of the above properties but together possessing all the essential physical properties showed a carrier efficiency higher than that of either constituent alone.

Besides diphenylamine the results were shown to apply to dioxanthogen  $\omega$ -nitrostyrene dibromide and rotenone but it does not necessarily follow that the carrier efficiency of a solvent is the same for all insecticides.

W A L David

KUHN H W OSBORNO-MESA E & BOSHILL MANRIQUE J Studies on Mosquitoes of the Genus *Haemagogus* in Colombia (Diptera, Culicidae) *Amer J Hyg* 1946 Jan v 43 No 1 13-23 1 fig & 6 pls. (1 coloured) [21 refs]

1 Eight species of *Haemagogus* were found in Colombia, 7 of them in the lowlands and one in the highlands.



PARROT L., MOKSET P & CADEWAT J. Notes sur les phlébotomes. L. Phlébotomes de l'Afrique Occidentale Française. 2 Guinée, Côte d'Ivoire, Dahomey [Phlebotomus of French West Africa: Guinea, Ivory Coast, Dahomey] Arch. Inst. Pasteur d'Algérie 1945 Dec. v 23 No. 4, 281-9 8 figs.

LATYSHEV N I. [Instructions for testing of Sandfly Repellents.] Med Parasit & Parasitic Dis. Moscow 1945 v 14 No 2, 82-5 [In Russian.]

The author points out that very little is known regarding chemical methods of protection against sandflies and discusses the methods of testing repellents and the results of some tests with sandflies. Observations on the efficacy of the repellents can be carried out by applying the chemical (1) to one side of the face or to one arm while leaving the opposite side of the face or the other arm untreated (2) to one individual and using a second one as control (3) to one part of a window leaving the other free (4) to whole groups of people with adequate controls. In the case of (1-3) the repellent effect is determined by comparative counts of sandflies while in (4) it is assessed on the basis of evidence of bites.

The following repellents have already been successfully used against sandflies (1) bis-ethylxanthogen (Preparation A. see also this Bulletin 1945 v 42, 940) used as a 3-5 per cent. solution in vaseline (2) 3 drops each of anise oil eucalyptus oil and turpentine, lanolin 30 gm. (3) turpentine 10 parts tar 4 Dalmatian powder and castor oil 20 of each lanolin and vaseline 40 of each (4) Japanese menthol 1 part, dilute carbonic acid 2 vaseline 100

Good results against other blood-sucking Diptera were obtained with wide-meshed nets impregnated with one of the following repellents and worn on the head (1) lysol 90 parts, turpentine 10 vegetable oil 5 water 55 (2) 5 per cent. solution of caustic potash to which 10 per cent. of tar is added. It is suggested that the effect of these repellents on sandflies should also be tested.

C A Howe

DELMANTO, A. Sobre a miíase oftálmica. Tratamento de sua localização intra-orbitária. [Myiasis of the Eye: Treatment.] Publicações Médicas. São Paulo 1945 Aug v 17 No 1 pp 17 19-21 23-4 2 figs

ARTHUR, W P. Habituation of *Pulex irritans* to Animal Host. [Correspondence.] Trans Roy Soc Trop Med & Hyg 1946 Feb. v 39 No 4 343-4

The author relates a personal observation which showed that *Pulex irritans* may become adapted to live on a dog. His spaniel was accidentally found to be infested with this species of flea, 100 being recovered from it. He had the dog on his knees and carried it in his arms but no fleas passed from the dog to infest him though he is ordinarily only attractive to fleas. The fleas were removed from the dog in an unoccupied room and some escaped when the author entered the purposely lighted room and four days afterwards the fleas bit him. A few fleas taken to infest the dog for over a year in spite of all the house of them. None of the other five occasions.

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F Corson

SERGEANT E. DONATIEN A. & PARROT L. *Expériences de protection des animaux domestiques contre la piqure des tiques par la poudre insecticide D D T* [The Protection of Domestic Animals against Ticks, by DDT] *Arch Inst Pasteur d'Algérie* 1945 Dec. v 23 No 4 249-59 4 figs

## LABORATORY PROCEDURES

LILLIE R. D. *Effect of Metals on Giemsa Stain Solutions in Fifty per cent Glycerol and Methanol Mixture.* *J Lab & Clin Med* 1946 Feb v 31 No 2 253-6

During the recent world war a batch of Giemsa stain solution deteriorated after the bottles had been issued to various places the eosin staining being lost. The bottles had screw caps lined with tin foil seals and these were noticed to have a yellow incrustation. The tin foil was later found to consist of tin (99.7 per cent.) with small amounts of lead, copper, arsenic, antimony and iron. Experiments were made with the tin foil and with various metals to see what effect they had on Giemsa stain solution as indicated by spectroscopic examination. The results are given in tables: it was found that various metals relatively active in the electrolytic series decompose thiazine eosinates in glycerol-methanol solution [Giemsa's stain] and remove eosin from the solutions. Alkali earth metals appear to act purely as alkalis. Zinc acts on methylthionins but not on thionin.

The authors conclude that tin foil or other foils containing tin, zinc or cadmium should not be used for lining screw caps for Giemsa's stain. Paraffined cardboard is satisfactory for the purpose. *J F Corson*

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

MEGAW J. *The Health of India.* *Brit Med J* 1946 Mar 9 343-7

This appraisal of the health of India by a recognized authority is concerned almost exclusively with the practically universal malnutrition caused by insufficient and unsuitable food. In countries in which malnutrition and infectious diseases have been reasonably well controlled, the average length of life has increased to well over 55 years. In India, where much has been done to control infectious disease but little or nothing to tackle the malnutrition problem, the average length of life is but half this figure. The control of epidemics has contributed to a prodigious increase in the rate of growth of the population. Between 1931 and 1941 the increase of population for the whole of India was 15 per cent, an actual increase of about 50,000,000. In parts of India the increase attained 22 per cent. The people must choose for themselves whether to adhere to the present system of unrestricted propagation of children with its attendant misery or voluntarily to apply an adequate check. The magnitude of the problem as set forth is staggering and this lecture was delivered before the imminence of widespread famine that faces India today was recognized. Increase in the production of food can scarcely keep pace with population increase unless drastic changes are made in outlook of life and manner of living. The abolition of uneconomic small holdings and the elimination of millions of useless cattle would be fiercely resisted.

The creation of a Commission is urged, to make an unbiased report on social and other customs which cause ill-health and economic depression in the rural population and to recommend suitable action to effect a change. The Commission should consist of enlightened Indians especially Indian women. Such a Commission might create a sense of danger needed to convince the people of the need for a change in their plan of life.

Norman White

WOOLLEY E. J. S. The Health of the Civilian Population of Tristan da Cunha. *J Roy Soc Med Ser* 1946 Jan. v 32, No 1 3-15 7 figs

Tristan da Cunha is no longer the *terra incognita* it was at the beginning of the century but this account is interesting in bringing information concerning the island up to date. The settlement has been in existence for 130 years and the population in 1944 was 122. Registers of marriages and births have been kept since 1871 and 1880 respectively and of deaths since 1892. The types of inhabitants range from whites with fair hair and blue eyes, to dark mulatto. The adults are of good physique the children and adolescents are not this is ascribed to deterioration in the standards of living for since there is less trade with passing ships the people have to depend more on their own efforts and the crops consist almost entirely of potatoes this food being supplemented by pumpkins fish and a few eggs of sea birds and fowls. Of late years there has been a little grazing, and consequently a little milk production. The island has no alcoholic drink. Living conditions are still primitive—houses of stone roofed with New Zealand flax or tussock grass sanitation is hardly existent. If buckets are used they are neglected as soon as they are full or are emptied in heaps near the dwellings.

Epidemics of colds and tonsillitis occur but there are no authentic records of any other epidemics if we except outbreaks of mild enteritis in the summer months when flies are a pest. Many suffer from local sores whitlows boils cellulitis impetigo which heal with difficulty and slowly. *Ascariis lumbricoides* is found to infect almost the entire population. The commonest disease is asthma (97 cases) next is fibrositis (18) and dyspepsia (11). In spite of the severity of the common cold, pulmonary disease is rare. Labour is usually easy and maternal mortality is nil children are breast-fed for a year or so but after 4 months they are given in addition potato and the infants are undernourished anaemic and dyspeptic. Hereditary deformities are noted nine descendants of one woman show deformity of the pinna, with partial or complete mental occlusion others showed polydactyly and "lobster hand". Intelligence is not easy to gauge because of the isolation of these people but 152 are said to be "normal" able to support themselves and their families and to be educationally receptive 43 are dullards feeble-minded improvident, lazy and lacking in initiative but capable of working under supervision nine are "high grade defectives." [This account of the general state and mode of life of these islanders makes gloomy reading—a marked contrast with the happy healthy lives of the early inhabitants of this former lonely Pacific island Pitcairn.]

H. Harold Scott.

BLANCHARD M. Quelques particularités de la pathologie de Madagascar [Remarks on Disease in Madagascar] *Les Grandes Endémies Tropicales*. (Onzième Année) 1939 Paris. pp. 5-13.

This is of the nature of a farewell talk by Inspector-General Blanchard. In it he refers in a few words to each of the following subjects. Plague yellow fever trypanosomiasis smallpox, and typhus in a group of infectious diseases. The chief point to note in this group is the possibility of introduction of yellow

fever. The author does not think that infective *Aedes* are likely to be brought in and the chief danger is from persons in the incubation or early stage of the disease. A second group he mentions is that of endemic diseases and here he refers briefly to malaria syphilis tuberculosis leprosy beriberi and rabies. The proposal has been made to decentralize large leprosaria and collect or re-group the inmates in small villages of 6 to 30 patients near medical centres and near their own homes. Other conditions briefly referred to in this paper are uratic deposits alcoholism intoxication by *Cannabis indica* the last of which is becoming more common as the price of tobacco rises. The only surgical condition spoken of is bites by caymans and in this connexion he cites a case which occurred in 1938. [The article is interestingly written but consists in the main of general remarks nothing new being contributed there are many things one would expect to find mentioned but they are not even referred to such as the use of the living E V strain of *P. pestis* in prophylaxis in Madagascar]

DAVID J. Une oeuvre française aux îles Wallis et Futuna [French Work in the Islands of Wallis and Futuna.] *Les Grandes Endémies Tropicales* (Onzième Année) 1939 Paris. pp 72-82. H. Harold Scott

VAUCEL. L'aspect social de la médecine aux Colonies. [The Social Aspect of Medicine in the French Colonies.] *Arch Méd Sociale* Paris 1945 Aug v 1 No 5 325-8

The author makes the point that in the colonies medicine is social in so far as it copes with diseases which are widespread and that for this purpose campaigns on a large scale are deliberately planned. [This recalls the remark made in Lord HALEY's *African Survey* that disease of the type which causes most mischief in Africa is generally a mass infection and must be attacked in the mass. See this *Bulletin* 1938 v 35 934] Instances of this kind of campaign are given. The sleeping sickness treatment services in West Africa examine 6 000 000 persons each year among whom about 20 000 cases of sleeping sickness are discovered annually. The epidemic has been stabilized and the infection rate is now about 0.5 per cent. For the prevention of yellow fever more than 10 million people have been vaccinated by the scarification method. In Madagascar extensive use has been made of the live E V vaccine in 10 years five million people have been vaccinated and the incidence of plague has fallen from 3,584 cases in 1934 to 184 in 1944. The author writes in general terms on the provision of a service of travelling units for the discovery treatment and prevention of the major diseases which should achieve a standard of efficiency much greater than is possible under the present system of fixed dispensaries.

DE BRIEY P. Migration of Indigenous Workers in the Belgian Congo. *Internat Labour Rev* 1945 Oct v 52 No 4 335-51 [Refs in footnotes] Charles H. Ilcocks

In an earlier paper Dr Margaret READ discussed the effect of the migration of African males from Nyasaland in search of work upon the communities left behind [this *Bulletin* 1942 v 39 723]. In the present paper de Briey discusses the same problem and the regulations formulated to deal with it in the Belgian Congo. The least harmful form of migration is the seasonal search for work when the men take employment for a short time only away from their homes. In this form there is relatively little interference with village economy and the men retain a strong connexion with their own communities. Much more serious in its effect on the men and on their families is the migration for work which entails absence from home lasting for 3 years or so especially if

the place of work is far from the village. Under these circumstances the men are suddenly placed in unfamiliar surroundings, to which they may react badly for themselves and their people. The age and sex balances of the villages are seriously disturbed if many men are away for long periods. The situation is less harmful if the place of work is near the homes of the workers.

The treatment of men detached from their home surroundings must obviously be considered with special care more especially if they have been recruited for work under conditions of which they have no exact understanding there are, therefore, special regulations governing the recruitment of labour. In the Belgian Congo measures have been taken to protect both the indigenous community and the indigenous worker. For the community from which the workers are drawn there is a land policy by means of which the Government tries to prevent the complete exhaustion of the labour supply in some areas by directing settlers from Belgium to areas where manpower is plentiful. There is also a social policy. The governor of a province may prohibit all recruitment of Africans if recruitment would mean that an undue proportion of men (over 10 per cent. of able-bodied men, that is over 2.5 per cent. of the whole community) were removed from the district. Reduction of the male population beyond this figure entails risk to the health and even to the continued existence, of the community. In formulating this principle the Government have taken into account that spontaneous application for employment does occur among the Africans, and that the number of persons thus actively seeking work is considerable. It is impossible to prevent those Africans from going to work who of their own accord, show that they wish to contract an engagement: the restrictions, therefore, apply only to active recruitment.

It is realized that if large concessions are made to Europeans in some areas the attractions offered to the Africans may be so great as to tempt away the whole male population from their homes. This would, however, not necessarily be so disastrous as recruitment because experience has shown that under some conditions the family of the African would accompany him. Nevertheless, the social consequences would be serious unless adequate steps were taken to provide for the welfare of these families in their change to a new life. "It is precisely the function of a colonial Government to create economic conditions tending to give the indigenous population a stable social environment adjusted to its degree of development." Attempts are therefore made by companies to stabilize the indigenous workers in their new surroundings by favouring long term engagements and by providing for the health and well-being of the

Periodical wage increments and bonuses for married men and those inducement to stay and to bring wives and families. Medical services are provided, in one case costing 10 per cent. of the total cost of indigenous labour employed. Education is also provided, and social institutions which cover a wide range of activities are encouraged. These efforts have been successful in creating new and stable communities. Stabilization will not abolish the evils which may attend the process of turning the tribal Africans into an industrial proletariat, but it will make them smaller.

The author concludes with the remark that whatever measures the Government adopts to deal with this complex problem success will depend on the human factor. [The line of thought that runs through this paper is very similar to that propounded by Sarr (this Bulletin 1948 v 43 257). The medical reader may draw the conclusion that since the impact of industry on the African will affect both his physical and mental health, it is the duty of Governments to seek the advice of their medical officers, much more than has in the past been the case, as to the measures to be adopted, and that the purely commercial point of view should not be given the priority it has too long enjoyed.]

Charles H. Necker.

WRIGHT SMITH R J A Case of Fatal Stabbing by a Stingray *Med J Australia* 1945 Dec. 22 v 2 No 25 466-7 2 figs

G P WHITLEY in his work on *The Fishes of Australia* describes six varieties of stingray in Victorian waters. The spine is strong and can be driven through the side of a boat and the fish can show great accuracy in stabbing. They often come into shallow waters for warmth and lie in the sands.

The case here recorded is that of a man of 33 years a powerful swimmer who when coming in from a bath suddenly showed symptoms of distress. He was helped in by friends and was breathing with difficulty. 20 minutes later he died. There was an oval shaped stab wound  $\frac{1}{2}$ -inch long at the fifth left intercostal space found at autopsy to have penetrated the pleural cavity and the pericardium and there was an irregular tear of the left ventricle  $\frac{3}{8}$ th inch in length near the apex. There was a smaller wound not penetrating beyond the subcutaneous tissue on the mesial side of the first. The pericardial sac was found to contain fluid blood and there was much blood and some clot in the pleural sac and haemorrhage round the wound in the left ventricle. The organs generally were healthy. The palings of the fence round the bathing place were broken and the stingray may have thus gained entrance. The water was dirty and nothing could be seen on the sea bed. No weapon spike or nail was found which might have caused the injury [but nor was any stingray].

H. Harold Scott

BULL. HEALTH ORGANIZATION (League of Nations) 1945/46, v 12, No 1 111-79  
The Unification of Pharmacopoeias. Interim Report of the Technical Commission of Pharmacopoeial Experts. (May 1945)

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## BOOK REVIEWS

**Manson's Tropical Diseases. A Manual of the Diseases of Warm Climates.**—Edited by Philip H. MANSON B.A., M.C., D.S.O., M.A., M.D., D.T.M. & H. Cantab. F.R.C.P. London Senior Physician to the Hospital for Tropical Diseases. London etc. Twelfth Edition.—pp. xiv+1068 17 colour pls. 9 half tone pls. 407 text figs. 6 maps & 29 charts. 1945 London Toronto Melbourne & Sydney Cassell & Co. Ltd. [42s.]

Manson's Tropical Diseases under the able and indefatigable editorship of Sir Philip Manson-Bahr goes from strength to strength. In the five years since the eleventh edition was issued there have been momentous happenings. Hundreds of medical men have been serving in the tropics for the first time and have met with diseases new to them, and differences in diseases with which they were familiar in temperate climates. These have rushed eagerly into print to record their experiences and the result has been a spate of literature, some of it of value, but much of it everyday matters to readers of this *Bulletin* with their extensive tropical experience. Also the fact of having large numbers of men fresh to tropical conditions under their care has afforded a unique opportunity for the more experienced to carry out research in the field on a large scale and to apply measures already tested and found successful in the laboratory. To sift all this vast amount of material, to separate the wheat from the chaff and present the wheat in a palatable and assimilable form has been the self-imposed task of the Editor and admirably has he performed it. He acknowledges freely and fully the help he has received from the Bureau of Hygiene and Tropical Diseases and its *Bulletin* and from the annual summaries of the previous year's

progress in all the important tropical diseases, which epitomize the abstracts made in the *Tropical Diseases Bulletin* on the several subjects during that year.

There is hardly need to review in full a work of such popularity as this. Its usefulness is obvious in the fact that a new edition has been called for every 4-5 years since it first saw the light and that in addition it has been reprinted no less than 17 times. Since the last edition was published in 1940 several matters which were then *sub judice* or obscure have been decided or solved necessitating modification in presentment. Suggestions then put forward for the consideration of the Editor have been carefully weighed and a number of them adopted.

In view of the developments in tropical medicine which have taken place in these five momentous years in the history of medicine and in particular of tropical medicine the Editor has found it necessary to recast some sections and to re-write others afresh to re-draw some of the illustrations and add new ones nevertheless, so ably has this been accomplished that though there are 43 more text-figures the whole book is 15 pages shorter than the 11th edition. New matter which is exceptionally welcome includes a chapter on the Technique of Injections and Blood transfusion and a list of special drugs used in the treatment of tropical disease more than a list for in the case of each we are given its common synonyms its chemical constitution and formula its therapeutic application and dosage. This is indeed, a boon but the section will need constant revision as new drugs are introduced some to replace old ones which will drop out, others to serve new ends.

To pass to matters of detail. There are signs on almost every page of most careful revision even to cutting out of single words to save space if the sense is not endangered thereby. Again, by printing two lines more on a page more space has been gained so that the new edition with more letterpress has even fewer pages than the last. This edition has 7 plates fewer than the preceding, we are sorry to miss the one depicting alastrum and that of the macular rash of leprosy. Whether it was wise to reproduce plates on both sides of a leaf is perhaps a matter of opinion, but the saving of less than half a score of pages is hardly compensated by placing some illustrations right away from their context as for example inserting the beautiful coloured plate of dysenteric lesions of the intestine in the pellagra section. The two pellagra plates could have been placed together and the dysentery one separate instead of one pellagra plate by itself and the other with the dysentery plate. Again the radiograph of calcified cysticerci comes in the guinea-worm section.

The part dealing with Food is a good summary of a difficult subject. Tropical anaemias are interestingly described but one fails to find reference to the pallor wrongly spoken of as tropical anaemia where there is no true anaemia. The risk of cooling drinks by addition of ice is not mentioned, though it is often done and may be a very serious risk. There is a peculiar slip on p. 29 which might be designated an accident of accident and another on p. 117 where  $\gamma$  is said to be equal to 0.0001 gm.  $\gamma$  = one-millionth of a gramme or 0.001 mgm. On p. 105 in Fig. 145 the male and female *W. bancrofti* have been transposed the formula of thiobismol (p. 52) needs a little correction.

The malaria section is one of those which have practically been re-written that on yellow fever is another. The list of malaria vectors has been both revised and much enlarged and there is also included a list of the regions of their typical breeding places. The typhus table has been remodelled and brought up to date the text here has been to a great extent re-written and now includes Lone-star (Bollis) fever and the account of the Q fever of Queensland is much fuller. The vitamin chapter has been expanded and almost entirely re-written. The inclusion of a table of syndromes characterized by glossitis and stomatitis was a happy thought. Other useful additions to which special attention should be directed are the improvement of the Glossitis table by

accompanying drawings of their distinguishing characteristics most informative also is the summary of the present state of trypanosomiasis in different parts of Africa, a short section on tick borne encephalitis has been added (p 618) A very valuable addition is the section on Technique of Injections Blood-transfusions etc already alluded to This is separate from the one on Laboratory Technique staining methods etc. usually included under the term Clinical Pathology

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In conclusion those who possess the eleventh edition are strongly advised to purchase this the twelfth, because it is almost a new work, for the changes are many and important and no one who intends to keep up with the times can afford to be without it. Also now that men are returning from service abroad a proportion of them suffering from or harbouring the seeds of tropical disease the general practitioner at home can no longer take up the attitude that such diseases do not interest him and are beyond his purview and he too should read this book with care and keep it on his shelf.

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H Harold Scott

PEREIRA O de Lofola. Contribuição ao Estudo do Tratamento da Lepre segundo os resultados obtidos em 10 anos de Terapêutica Antileprótica na Leprosaria Central de Gôa. [The Treatment of Leprosy and its Results at the Central Leprosarium at Gôa.] *Supplement No 2 to An Inst Med Trop* Lisbon. 1945 Nov 147 pp 1 fig [246 refs.]

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references to writers of all nationalities is given and more than half (129) are to abstracts which have appeared in the *Tropical Diseases Bulletin* indicating how useful foreign writers find this publication.

In the first part which occupies one-third of the thesis the preparatory treatment is considered and discussed, attention being drawn to obtaining the hearty co-operation of the patient seeing to his food and nutrition to his physical exercise his mental occupation and distractions, and the treatment of concomitant or intercurrent disease, such as malaria scabies influenza etc.

The Central Leprosarium of Gôa (India) was opened in May 1932, in a fairly isolated rural spot, Macasana in the Salcete Municipality and it is divided into two parts one occupied by the lepers the other by the staff their families and dependants. At present there are 100 resident patients. In 1935 there was an outbreak of malaria and 34 of the lepers were attacked. — The malaria did not seem to affect the leprotic infection in any way nor *vice versa*. Twenty four received vaccination against smallpox and in 15 of them the small operation was followed by a leprotic reaction—aggravation of lesions especially those of the nerves and the nodules and glands swelled—which led to much debility and prolonged time of convalescence in half the patients the vaccinia pustule became an ulcer which in some cases took several weeks to heal this was specially noted in those who showed a marked leprous reaction.

In the second part the author considers the many forms of treatment tried in leprosy. He deals in turn with chaulmoogra, the oil and its derivatives its administration *per os* *per cutem* intramuscularly and by the blood-stream, the use of the whole oil and of its ethyl esters and of the combination of chaulmoogra with cholesterol. Next with serum therapy Reenstierna's serum and antitetanus serum, with vaccine therapy vitamins, sulphonamides venoms, dyes and chemotherapy. Abundant quotations from the literature are given on each of these and then remarks on the cases in which the author has himself tried the method. The numbers are, as a rule, too small to be of any statistical value in gauging results but when added to those of others they may be of some value and anyway are an expression of the opinion of the author.

For oral administration refined chaulmoogra oil is given in gelatin capsules, containing 30 minims each. For the first week in each month one capsule daily is prescribed, for the second and third weeks two capsules daily for the fourth week none. The cutaneous route is objectionable because of the odour imparted to the body and clothes. Intramuscular injection is the favourite mode of administration and three cases are quoted one received 33 injections in seven months, when death took place by which time the leprosy had slightly improved. A second had only two injections when the onset of cardiac disturbances necessitated a stop the third had 25 injections and was slightly improved. For ethyl ester injections the author used E.C.C.O.—ethyl esters of the oil of *H. wightiana* 1 cc., camphor 1 gr. doubly distilled creosote 1 cc. and olive oil 2.5 cc. This is the method chiefly used in the Gôa leprosarium. Three cases are quoted one man received 377 injections and then died. The drug had no effect on his disease. A second received 23 injections in 4½ months, together with Moogrol and was "clinically cured, but was continuing treatment a third was treated similarly and had improved. Sixty two patients were treated with intravenous injections (up to 70 injections) of Alepol 11 of them improved, 5 became worse and 46 remained in their original state.

Ten lepers were given the Reenstierna serum in three or four series of 2-3 intramuscular injections with 5-10-week intervals between the series. The injections were followed by considerable physical depression in all three improved, one was worse and six remained unaffected.

One case is recorded of a patient who developed symptoms of tetanus trismus convulsions opisthotonus etc. and was given antitetanus serum. To the author's surprise the leprosy nodules shrank the infiltrations and anaesthetic patches diminished and ulcers cicatrized. [It is a pity that this serum was not tried in other cases to confirm or refute whether this was purely incidental.]

Eleven were given Vaudremer's vaccine subcutaneously in increasing doses and good effects were observed in those with oedematous infiltration of hands and feet with elevation of temperature and general weakness for those with eye lesions special caution is to be exercised in its use. Betaxan was found to benefit those with polyneuritis and joint pains in eight patients Sulphonamide drugs were tried in a few cases but did not seem to bring about any amelioration. For animal venom the toad (*Bufo bufo*) was tried on some cases of nodular leprosy no benefit resulted. The dyes used for treatment were methylene blue (1 per cent. in distilled water starting with 5 cc. and gradually increasing till 35 cc. might be given at one time) brilliant green crystal violet trypan blue fluorescein eosin resorcin gentian violet erythrosin fuchsin acridin methyl green among others the numbers of cases so treated are not stated but the statement is made that amelioration followed in several

The author sums up his opinion in the following paragraphs Chaulmoogra gives the most certain results it is best administered in the form of the pure oil neutralized good results were also obtained with Leprosan a product of Taraktogenol A Alepol was generally disappointing but seemed to do most good in those of mixed type with skin lesions prominent a mixture of chaulmoogra and cholesterol injected intravenously is well tolerated but the practical result is doubtful Reenstierna serum proved best in rhinitis cases and those with anaesthetic and infiltrated areas Vaudremer's vaccine is specially indicated for those with oedematous infiltrations of the extremities toad venom was good in leprosy adenitis and neuralgias in which benefit was often prompt sulphonamide drugs find no place in the treatment of leprosy Vitamin B<sub>1</sub> benefits those with neuralgias and joint pains methylene blue caused disappearance of large dyschromic blotches but had no effect on a nodular case mercurochrome intravenously was of benefit in lepromatous ulcers.

H Harold Scott

MOOSER, Hermann. [Professor an der Universität Zurich.] Die Beziehungen des murinen Fleckfiebers zum klassischen Fleckfieber [The Relationship of the Murine Typhus Fevers to Classical Typhus.] *Acta Tropica* Basel. 1945 Suppl. 4. 87 pp 1 pl. & 1 chart. [171 refs.]

In this volume of 87 pages including a bibliography of 171 references the author recapitulates his reasons for holding the following views —(1) Contrary to the opinion of NICOLLE there is only one murine typhus (2) The differences between *Rickettsia prowazeki* and *R. mooseri* are quantitative and not qualitative. (3) These differences however are regularly observed and must be regarded as specific.

The quantitative differences are regarded as being heterologous protection with vaccines scrotal phenomenon in the guineapig pathogenicity for white mice and seral transfer in mice and rats In these respects there is merely a disproportion between the pathogenicity and serological activity of the two strains Some strains of classic typhus cause scrotal lesions in guineapigs and some can be transferred in series through white mice when large doses of infecting material are used.

Contrary to the claims of NICOLLE and GIROUD *R. mooseri* develops in lice exactly as does *R. prowazeki* and there is no difference between the two with respect to their multiplication in fleas.

The assumption that classical typhus has originated from murine typhus remains an unproved hypothesis and those who refuse to accept this hypothesis can choose between Zinsser's view that infection is carried over in inter-epidemic periods by late relapses and the assumption of Polish workers that the carry-over is by dried faeces of infected lice. Nicolle's hypothesis of a carry-over by inapparent infection is regarded as having been disproved by the author's work in Mexico.

The author again suggests that fleas may play a part in maintaining *R. prowazeki* outside the human body and so in maintaining infection during inter-epidemic periods. In support of this view are the facts that the organism multiplies just as readily in fleas as does *R. mooseri* and that the life span of the fleas is not shortened by the infection.

Great stress is laid on the importance of the work done by the author and his colleagues in Mexico in throwing light on the significance of the rickettsial bodies which are stated to have been of a doubtful nature till 1931. [It seems surprising that serious doubts could have been entertained on this subject after the appearance of the classical work of Wolbach and his colleagues (see this Bulletin 1922, v 19 448) in and before 1922.]

The author claims that much of the recent work on the rickettsiae is merely a rediscovery of the findings made earlier in Mexico and the U.S.A.

The general tone of the book is sharply critical especially of Nicolle and Zinsser who unhappily are dead. But although this unfortunate circumstance puts the author in an invidious position, he cannot be blamed for speaking plainly in the interests of what he regards as scientific truth. A disturbing impression conveyed by the book is that some widely accepted generalizations connected with epidemic and murine typhus are shown to have been based on inadequate and slender evidence.

No reference is made to the important recent work on the complement-fixation and rickettsia-agglutination reactions in epidemic and murine typhus but this could hardly be expected in a book which consists largely of a vindication of the author's work about whose importance there can be no dispute.

John W. D. Aitken

WAR DEPARTMENT WASHINGTON Insect and Rodent Control. Repels and Utilities. War Dept. Technical Manual TM 5-632 Wash. 1943 Oct. pp. iii+135 100 figs. [Numerous refs.]

This publication of the United States War Department is of quarto size printed in large type on good paper and is profusely illustrated with photographs and diagrams. Short descriptions of the chief insect and rodent pests and of the various methods of controlling them are given. The insect pests include mosquitoes house flies bed-bugs lice fleas ticks, chiggers (mites) termites (white ants) cockroaches beetles and ants the rodents are rats mice ground squirrels and pocket gophers moles coyotes and foxes are also mentioned.

The methods of control described and illustrated are the recognized major and minor sanitary measures—drainage screening spraying and oiling trapping, poisoning, fumigation and the protection of buildings against rodents and termites.

Emphasis is laid on the importance of co-operation of Army Departments—Medical, the Corps of Engineers and the Quartermaster Corps with each other and with the specialists of the Public Health Services the Navy Department, the Department of Agriculture and the Department of the Interior.

The book will be interesting and valuable to all who come into contact with these pests as well as those whose duty it is to deal with them.

J. F. Corson

# TROPICAL DISEASES BULLETIN

[Vol. 43]

1946

[No. 7]

## THE TREATMENT OF AMOEBIASIS

### A REVIEW

By A. R. D. ADAMS M.D. Ch.B. M.R.C.P. D.T.M.

#### *Emetine*

The specific treatment of amoebic dysentery dates back some three centuries when ipecacuanha was introduced to Europe from South America as a remedy for dysentery. The employment of the drug was at first entirely empirical and it was not until 1912 that ROGERS [this *Bulletin* 1912 v 1 176] showed that the alkaloid emetine exerts a potent action on *Entamoeba histolytica* which had been recognized by SCHAUDINN in 1903 as the causative parasite of amoebic dysentery. The treatment of amoebiasis was thereafter established on a more rational basis and emetine in one form or another has since been recognized as an essential component of any course of treatment for the acute clinical manifestations of *E. histolytica* infections.

From the time of these early experiments it has been known that emetine alone will not cure that is completely eradicate more than a relatively small proportion of *E. histolytica* infections of the large intestine. What this proportion is has been the subject of some discussion: it is generally agreed to be not more than one third of those so treated (CRAIG: Amoebiasis and Amoebic Dysentery, 1934 (London: Baillière Tindall & Cox p. 276) puts the figure at between 10 and 15 per cent.) but there is room for a more precise evaluation of the drug as a curative agent if given in full dosage during primary clinical attacks of amoebic dysentery. The view is now widely held that the use of injections of emetine in intestinal amoebiasis should be confined to the arrest of acute manifestations and that when these have been controlled the emetine injections should be stopped: it is considered pointless to continue them indefinitely or until a specified number have been given as a routine. One injection each day for 4 or 5 days will usually achieve the desired result and 12 injections will do no more. The salt of emetine employed for intramuscular or hypodermic injection is the hydrochloride and the dosage is 1 grain daily for an adult: this dose may be divided  $\frac{1}{2}$  gr. being given at intervals of 12 hours but there is no obvious material advantage in this procedure. A patient receiving emetine injections should be confined to bed. Gross toxic effects are rarely seen from the use of the drug in normal dosage if it is not continued for more than 10-12 days. The toxic manifestations to be watched for in practice are a rising pulse rate, irregularity in the heart's action and a fall in blood pressure. If these develop the drug must be stopped. Peripheral

neuritis, with wrist and foot-drop and even death may occur but these are rarely encountered except when the dosage has been injudicious and the course unduly prolonged. Emetine should never be given intravenously.

### Metastatic Infections

In addition to their rapid action in controlling acute clinical exacerbations of amoebiasis due to primary infection in the gut, emetine hydrochloride injections act specifically in arresting and in most cases in eradicating secondary amoebic infections in other organs and tissues, provided that treatment is not unduly delayed. In liver infections the parasites are usually destroyed by one course of a dozen daily injections of emetine hydrochloride and this is equally true of infections of the lung, of the skin, and of those direct extensions of the infection from intestinal lesions to neighbouring organs and structures which result in the formation of amoebic granulomata (amoebomata) in the abdomen. Where such diffusions of the infection from the primary focus in the large bowel occur a course of 12 injections of emetine one a day should therefore be given at once to kill the amoebae in the secondary lesions. Surgical intervention may also be necessary but this can usually be averted if the condition has not been allowed to develop too far before the emetine is administered. It is wise to adopt a conservative attitude to surgery and to await developments before deciding on operative interference. Remarkably large amoebic liver abscesses, so long as they are bacteriologically sterile, are often absorbed when the causative parasites have been destroyed by emetine treatment. Where evacuation of an amoebic liver abscess is deemed necessary open drainage of the cavity is now generally held to be preferable to aspiration the latter usually has to be repeated, and often proves inadequate, so delaying the more radical procedure. In no case where surgery is resorted to must the fundamental sterilization of the lesion by peritoneal emetine injections be overlooked or the erosive process will continue and the parasitic infection will extend into the tissues involved in the operation. There is no point in putting emetine into the abscess cavity where it acts as a local irritant and does not appear to reach the tissues infiltrated with parasites around the lesion. Where such secondary infections in the large intestine and that the forgotten that the primary infection is in the large intestine and that the successful treatment of the secondary lesion leaves this primary infection, in most cases, unaffected.

### Treatment of the Intestinal Infection.

The eradication of an *E. histolytica* intestinal infection, whether the patient be harbouring a symptomless infection, and passing formed stools containing the cystic form of the parasite, or be suffering from recurring frank amoebic dysenteric attacks with the passage of blood and mucus, containing the vegetative stage of the parasite is in general, easy of achievement. A number of drugs administered by the mouth or in the form of colonic retention enemata, are employed for the purpose, although none of these can be claimed as entirely specific, in that each given alone fails to cure a considerable proportion of cases. It is a common practice, in view of this, to use several drugs concurrently or in sequence, in the belief that their combined action is greater than that of any single one of the series, and the "combined treatments" of various authors [this Bulletin 1945 v 42, 559 731 695 and 699] are the result. These treatments, broadly have much in common and in most cases of latent amoebiasis, and of early previously untreated relapsing amoebic dysentery are all effective in eradicating the infections. There seems to be no substantial evidence that any one of the courses is greatly superior to the others, provided that the

drugs are given so that they are liberated and retained for an adequate time in the correct part of the gut. MANSON, BAHR [this *Bulletin* 1945 v 42 207] directs attention to the importance of the selection of drugs in a suitable form and of their proper administration in order to obtain satisfactory results. The drugs usually employed consist of an emetine preparation for oral administration (emetine-bismuth-iodide Auremetine) a trivalent arsenical similarly given (Stovarsol Carbarsone) and one of the iodo-oxy-quinoline series (Diodoquin Enterovioform Chiniofon) for oral use or as a colonic retention enema.

Toxic complications sometimes result from the administration of the arsenicals to susceptible individuals which usually at first take the form of skin eruptions and reduction in the dosage or withdrawal of the drug will arrest the trouble. Very occasional deaths have been recorded from arsenical poisoning may occur if the drugs are continued, grosser manifestation of arsenical poisoning may occur the arsenicals and even of Carbarsone which is usually regarded as the least toxic of them [MAYER *Lancet* 1946 April 27th 631].

For the treatment of a symptomless carrier of the infection the procedure would consist of the administration of one of the combined courses referred to above. For the treatment of an early uncomplicated and previously untreated case of relapsing amoebic dysentery seen during an acute exacerbation of the disease the procedure would be the administration of emetine injections for three or four consecutive days to arrest the clinical attack immediately followed by a combined course to eradicate the infection. In a case of amoebiasis complicated by a secondary lesion such as early embolic infection of the liver twelve daily injections of emetine would be given to sterilize the liver lesions and a combined course of treatment to sterilize the gut necessary the combined treatment of the intestinal infection might well be delayed after completion of the emetine injection course until the patient was convalescent from the operation but there should be no undue waste of time in tackling the intestinal focus.

#### Criterion of Cure

The criterion of cure of an intestinal *E. histolytica* infection is the continued complete absence of parasites from the stools after treatment. For a week or two after unsuccessful intensive treatment parasites will probably be too few in number in the stools to be found microscopically. Stool examinations should therefore be deferred for a couple of weeks after conclusion of the treatment and at least a dozen specimens taken on consecutive days should then be searched for parasites. If this search is competently made and no *E. histolytica* is found, the presumption of cure is considerable though not absolute. Certain cases of persistent infection may escape notice and where possible in order not to miss these serial stools should subsequently be examined at intervals over a period of at least twelve months.

#### Refractory Cases

During recent years a considerable number of men were invalided from the various war fronts in the East with severe relapsing amoebic dysentery which had yielded only temporarily to the treatments available under fighting conditions. Many of these men had received very large numbers (100 or more) of injections of emetine hydrochloride and some had in addition been treated with the arsenical or iodo-oxy-quinoline series of drugs. Some of these cases proved refractory to any of the combined courses of treatment referred to above even after repetition on several occasions although they temporarily



benefited from them in that the clinical manifestations of their dysentery abated, the intestinal infection was not cured, and clinical exacerbations of dysentery recurred, usually in severe form within a few days or a week or two of completion of the course. Such cases it is held by some workers had developed resistance to emetine as a result of the undue amount of this drug given them while in the field but while there is some clinical evidence that emetine-resistance may occur in individual cases of amoebic dysentery the development of emetine-fastness in a strain of *E. histolytica* has not yet been conclusively demonstrated *in vivo* or *in vitro* and its existence is still subject to proof. Nevertheless it is probably sound policy to assume that it may occur and to forestall it by avoiding prodigal and needless resort to emetine injections in the treatment of amoebic dysentery.

### *Associated Bacterial Infection of the Bowel Wall*

Another explanation of the difficulty experienced in sterilizing some chronic relapsing amoebic dysenterics of their parasites is the establishment of an extensive concurrent bacterial infection of the tissues of the gut wall. On microscopical examination of the stools of such individuals pus will usually be found, and on sigmoidoscopy ulceration and a generalized inflammatory condition of the mucosa may be seen. A secondary bacterial colitis is coincident with the primary amoebiasis and thus concomitant bacterial colitis probably renders the amoebic dysenteric infection more difficult to eradicate. The colitis not infrequently persists as a chronic post-dysenteric colitis after the successful eradication of the amoebic infection. That its presence makes the amoebiasis more resistant to treatment is to some extent substantiated by the experience of certain workers who either prior to or concurrently with, a combined course of treatment for the intestinal amoebiasis now give a therapeutic course of one of the sulphonamide drugs (sulphaguanidine succinyl sulphathiazole or phthalyl sulphathiazole) or of penicillin in massive dosage or of both with improvement in the cure-rates for the amoebiasis in such cases. When a patient has proved refractory to previous treatment or has suffered for long from an untreated relapsing amoebiasis, or when pus is found in the stools or there is sigmoidoscopic evidence of a diffuse inflammatory or ulcerative condition of the large bowel such preliminary treatment with a sulphonamide drug or penicillin or both, is advisable. HARGREAVES [this *Bulletin* 1945 1 42, 559-595] has claimed very good results with an initial dose of 100 000 units of penicillin intramuscularly followed by 33 000 units every 3 hours to a total of one or two million units and succinyl sulphathiazole to a total of 80 gm. by the mouth. The writer's practice is to give succinyl or phthalyl sulphathiazole and Chlorsolon each by the mouth, on alternate days for ten days prior to combined therapy in such cases and he has not found penicillin so generally effective as has Hargreaves in relieving or arresting a severe bacillary colitis. It is to be clearly understood that the sulphonamides and penicillin have no direct action on the amoebae their action is exerted on the secondary bacterial invaders. Nevertheless evidence accumulates that control of a gross secondary bacterial invasion of the wall of the large intestine leads to more effective action of any treatment directed against the *E. histolytica* infection.

### *Diet and Management.*

There is general agreement also that a liberal nutritious, easily assimilable and palatable diet is of benefit in these cases, and that adjuvants in the form of vitamin concentrates may play a part in promoting bodily resistance. Whether confinement to bed throughout combined treatment is necessary or desirable must be determined by the circumstances of each individual case.

Complicating infections should be dealt with and the general condition be maintained at as high a level as possible. Abstinence from the bulkier alcoholic drinks is advisable and the maintenance of the morale of patients suffering from such a disease is an important factor in their successful treatment, as willing co-operation is of fundamental importance to its achievement.

Finally when the amoebiasis has been successfully eradicated, any troublesome sequelae such as the haemorrhoids commonly found in association with a diarrhoeic disorder must receive attention before the patient is discharged as cured.

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## SUMMARY OF RECENT ABSTRACTS \*

### VI. PLAGUE.

#### *Epidemiology Transmission*

In *Public Health Reports* (p. 32) is a record of the only human case of plague notified in the United States during 1943. This case in a child aged two was unusual in that death took place two months after onset and was due to bubonic plague with chronic plague encephalitis. Plague is widespread in rodents in the United States.

In the *Epidemiological Information Bulletin* of the Health Division of UNRRA (p. 724) there is an account of an outbreak of plague in Western Yunnan near the Burma frontier where plague has long been endemic. Most of the patients had received one or more inoculations of vaccine but though this had not been enough to prevent infection the death rate in the vaccinated was much lower than in the non vaccinated [see also MÜNTER below]. Sulphadiazine in a small series of cases appeared to give better therapeutic results than sulphathiazole or serum.

SMITH and POLLITZER (p. 725) have calculated the point at which the incidence of plague in the rat population of central China becomes a serious threat to man. They have found that the situation is reassuring so long as the incidence of infected rats is well below 20 per cent but human plague is imminent if a level of 25 per cent is reached.

POLLITZER and LI (p. 726) discuss the decline of epidemics of pneumonic plague in China. The principal factor seems to be the diminishing incidence of cases with cough and bloody sputum teeming with bacilli. The danger of infection from patients with plague pneumonia but without bloody sputum is much less than from those with the classical signs.

LE GALL (p. 280) contributes an account of plague in Madagascar making the point that the incidence rose to a high level about 1932 and fell rapidly after the institution of vaccination on a large scale, with the live E.V. vaccine. Pneumonic plague is common in the high plateau region and is a respiratory disease of direct transmission. For bubonic plague *X. cheopis* is the usual vector and this flea can live for some time away from rats for this reason the rat flea index is not now regarded as important in epidemiological studies. Continued examination of captured rats for plague infection seems now to be superfluous in Madagascar. Treatment with E.V. anti-plague serum and sulphonamides gives good results in bubonic plague but not in the pneumonic infection.

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\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945 v. 42. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

BLANC and BALTAZARD (p. 33) quote an experiment which, in their view tends to discredit the theory that blocking of infected fleas is an important factor in the transmission of plague. A group of *Xenopsylla cheopis* were infected, and remained infective during a span of life which did not differ from the normal. If transmission is a function of blocking, and if, as is usually supposed, a blocked flea does not live long, it would appear that the fleas became blocked successively which is unlikely. The authors think, rather, that the principal factor in transmission is the multiplication of bacilli in fresh blood taken up in frequent feeds. An infected flea, after a fast of 15 days, is unable to infect by its first bite, but becomes infective less than 12 hours later. This view is supported by experiments on other arthropods in which blocking does not occur. It has a bearing on human plague, since *X. cheopis* attacks man only when urged by hunger. The same authors (this Bulletin 1944 v. 41: 251) maintain that, in Morocco transmission of plague from man to man by *Psylla irritans* is by no means uncommon. GIRARD (p. 375) discusses this question, and concludes that although the prevalence of *P. irritans* may create special infective conditions in Morocco the really important vector in general is *X. cheopis*. He upholds the view that blockage of the proventriculus, which occurs in *X. cheopis* but not in *P. irritans*, is an important factor in transmission.

Girard makes the point that *X. cheopis* may exist for long periods away from the rat (see LE GALL above) and emphasizes the overriding importance of eliminating contact between rat and man, in the control of plague. In reply to Girard, BLANC and BALTAZARD (p. 376) uphold the two propositions that the human flea and house usually become infected on man in the agonal period, and that they can transmit plague. They point out that *P. irritans* is strikingly averse to biting guinea-pigs, and that this fact has vitiated much laboratory experimental work. It will, however, bite man freely.

HECHT (p. 251) has shown that although in part of Venezuela *Rhopalosiphum* is usually the most common flea on trapped rodents, there is from time to time a considerable increase in the proportions of *X. cheopis* and *X. brasiliensis* caught.

JELLINEK (p. 305) records the host relationships and geographical distribution of fleas of the genus *Oropsylla* in North America.

In a survey of sylvatic plague in part of Argentine SAVINO and KUSNETZ GONZALEZ (pp. 33-465) found natural infection in *Gracorys grassoflexus centralis* which is known to have contacts with human habitations, and in several cats.

SAVINO *et al.* (p. 555) describe a chronic encapsulated abscess, containing living plague bacilli, in the spleen of a rat. This is a very rare condition, and may indicate the means by which infection is carried over from one plague season to the next.

### Pathology

MACCIELAVELLO and UNGER (p. 468) think that although invasive capacity and toxicity of *P. pestis* are to some extent interdependent, they may differ quantitatively. Strains from the Andean region of Ecuador are highly invasive, belong to the S and not to the R form, are of relatively low toxicity and are peculiarly pneumotropic. It seems that the very mildness of plague in that region allows time for the production of secondary pneumonic plague, to a greater extent than elsewhere.

DEVIGNEY (p. 876) reports a sudden chromogenic disassociation, perhaps even a mutation, giving colonies of typical R and S type, with yellowish coloration, in the E.V. strain of the 104th passage.

WOODWARD (p. 281) has shown that *P. pestis* has an action in decomposing the ribonucleic acid of yeast.

### *Treatment*

A case of laboratory infection with plague is reported from San Francisco (p 33) [this is presumably the case referred to by MÜNTER, below]

Recovery from primary pneumonic plague is very rare. MÜNTER (p 805) reports the case of a doctor in the United States who was engaged on plague investigation and who about one year before he contracted plague pneumonia had received five injections of plague vaccine. The diagnosis of plague pneumonia was completely established, and treatment with sulphadiazine was instituted at an early stage the patient recovered and the very careful precautions taken to prevent spread of the disease to those who attended him were entirely successful. The author makes the point that recovery cannot be attributed solely to the action of the drug since other factors e.g. the vaccination may have contributed to the favourable result [see the UNRRA report above]

In an alternate-case trial of sulphadiazine and sulphathiazole in plague in an adequate series of patients WAGLE (p. 558) has shown that though each drug is valuable sulphadiazine is considerably more effective than sulphathiazole the case mortality rates in the two series were 21.9 and 33.7 per cent, respectively when no differentiation was made between septicaemic and non-septicaemic cases and 12 and 21 per cent when patients moribund on admission were excluded. The dosage for sulphadiazine was 10 gm the first day, and 6 gm on subsequent days. DE VILLAFANE LASTRA (p 892) treated 35 patients (four of whom had septicaemic plague) with sulphathiazole in high dosage 10-12 gm. daily for adults giving a blood level of over 8 mgm. per 100 cc. for not less than 6 days. There were five deaths all in patients with bubonic plague and in four of these plague meningitis was present.

The case mortality rate from plague in part of Hawaii between 1910 and 1944 was almost 100 per cent compared with 49 and 32 per cent in San Francisco and New Orleans. WILKIN and WILBAR (p 642) therefore investigated the therapeutic effect of penicillin experimentally in Hawaii all the guinea-pigs died and the result was wholly disappointing.

MACKAY DICK (p 377) notes a series of severe urticarial reactions in British soldiers who received injections of anti plague serum none of the Indians similarly treated showed this effect.

### *Control Vaccination*

HUMBLEY and NAST (p 282) recall that plague was found in Tacoma in rats for the first time in 1942. An intensive campaign was undertaken and so far as can be determined the infection was brought under complete control at a reasonable cost. The measures included trapping poisoning gassing fumigation food sanitation harbourage elimination rat proofing quarantine and educational activities. SHIH *et al* (p 726) describe the measures taken to control plague in two small towns in China.

In an investigation into the immunizing power of living attenuated vaccines in plague HSUE (p 726) concludes from animal experiments—that dead vaccines are unsatisfactory—that attenuation of virulent bacilli can be effected by continual subculture at 41-42°C. that a spontaneously attenuated strain had much better immunizing power than artificially attenuated strains and that antigenic potency of living vaccines is higher the further they diffuse into the internal organs from the site of injection.

ABRAMOVA (p 642) shows that vaccination with an avirulent live strain of *P. pestis* causes an increase in the opsonic index of animals but in his experiments correspondence between the degree of immunity as tested by subsequent virulent inoculation and the opsonic index was not exact.

It has long been known that guinea pigs rendered partly but not completely resistant to plague by injection of vaccine or immune serum are especially liable to death from secondary plague pneumonia after virulent infection. GIRARD (p. 377) raises the question whether the prevalence of pneumonic plague in Madagascar can be explained by some such mechanism the result of the extensive use of live E.V. vaccine and whether a state of incomplete immunity could restore the virulence of the living organisms of which the vaccine is composed. He answers these questions in the negative, showing that pulmonary complications are not more common in the vaccinated than in the unvaccinated, and that the incidence of pneumonic plague has diminished in Madagascar *pari passu* with the total incidence of all forms of plague. Man, therefore appears to differ from the small rodents in liability to plague pneumonia after insufficient immunization. *Charles Walcotts*

## MALARIA.

RUSSELL, P. F. Lessons in Malaria from World War II. The Charles Franklin Craig Lecture 1945. *Am. J. Trop. Med.* 1946, Jan. v. 26 No. 1 5-13. [14 refs.]

BELTRÁN E. Notas críticas sobre terminología paludológica. [Critical Notes on the Terminology of Malaria.] *Bolet. Oficina Sanitaria Panamericana* 1945 Oct., v. 24 No. 10 879-90. [16 refs.]

BEIERER, W. B. Malaria and Socio-Economic Conditions in Mississippi. Reprinted from *Social Forces* 1945 May, v. 23 No. 4 451-9. 4 graphs.

In establishing a definite relationship between socio-economic conditions and malaria mortality from year to year in the State of Mississippi, the author deals with a neglected aspect of malaria epidemiology. The prosperity of Mississippi is mainly dependent upon cotton cultivation. Cotton tenant farmers are among the poorest farmers in the United States—in many areas they live at subsistence level, their existence depending upon the price of a single commodity. The cotton-growing areas have an inadequate supply of food crops and their inhabitants live on a meagre and ill-balanced diet. There is a definite relationship between the price of cotton (retarded for one year) and net return from personal income tax, and malaria mortality in the State from year to year. During years in which income is high the people have more and more varied food, their homes are kept in better repair especially in regard to screening, and if suffering from malaria they have money for medical services and adequate antimalarial drugs. During years of low income the reverse is the case.

About 950,000 people of the 3,100,000 population of Mississippi are in the tenant farmer group. They have nomadic habits—29 per cent. of them operate the same farm for only one year or less, then they move on in search of a better job. Eighty per cent. of all tenant farms are occupied by farmers who have been on the farm for less than five years. This mobility accounts in some measure for the low socio-economic level.

In Mississippi socio-economic conditions appear to explain adequately the cyclic exacerbations of malaria every five, six or more years which have characterized the disease in the southern United States. *Norman White*

BRIERLY W B The Influence of Surface Features upon the Distribution of Malaria in Northwestern Mississippi. Reprinted from *J Geography* 1945 Nov \ 44 No 8 312-24 3 figs

The influence of physiographic conditions in determining variations in malaria incidence is well illustrated in this study. The delta region in north west Mississippi is a flat monotonous plain. It slopes only four or five inches to the mile southward and eastward and contains innumerable swamps and other collections of water favourable for the breeding of *Anopheles quadrimaculatus*. The Loess Bluff Upland which borders the delta region to the east is a rough rolling hilly area with relatively few hydrographic features. Malaria is much more prevalent in the delta  
Norman White

LE GAC P SEITE P & COMBES OT DE MARSAGUET G Étude sur le paludisme à Ouagadougou (Study of Malaria in Wagadugu.) *Bull Soc. Path Exot* 1945 \ 38 Nos. 78 201-16 1 fig

A severe outbreak of malaria in Wagadugu at the close of 1941 and the beginning of 1942 prompted the malaria survey, the results of which are here recorded. (Wagadugu is the capital of Mossi in French West Africa just north of the Gold Coast Colony.)

An examination of 2 942 children from 2 to 12 years of age during the rainy season June to October revealed a spleen rate of 37.15 and a parasite rate of 53.67 per cent. The corresponding rates for 808 children in 7 adjacent villages were 44.55 and 50.49 per cent. The gametocyte rates of these two groups of children were 14.81 and 22.76 per cent. *P. falciparum* was responsible for 93 per cent of infections, the remainder being due to *P. vivax*. *P. malariae* was not found.

Three species of *Anopheles* were found: *A. gambiae*, *A. funestus* and *A. nili*. *A. gambiae* is much the most prevalent. Marigots constitute the chief breeding places. (A marigot is a river that loses itself in the ground, often dry in the dry season; it is subject to flood in the rains.) In Wagadugu certain of the marigots are dammed so as to contain water throughout the year. The laterite soil favours the creation of temporary breeding places suitable for *A. gambiae* breeding. Of anopheline breeding in marigots only 5 to 6 per cent. are *A. funestus*, the remainder being *A. gambiae*. *A. nili* breeds in wells in which 72 per cent of the anopheline larvae taken were of this species. In Wagadugu there are some 1 880 wells, never more than 10 to 12 metres in depth and generally dry for two or three months in the year. Anopheline larvae were found in 452 of the 1 880 wells examined. Wells dug or drilled to a greater depth, tapping an underlying sandy stratum, are capable of supplying abundant pure water all the year round and would obviate the necessity of relying on marigots for the supply, as hitherto.

The very great scarcity of oils for use as larvicides contributed to the exceptional severity of malaria in 1941-42  
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RIBBARDS C R Moonlight and House-Haunting Habits of Female Anophelines in West Africa. *Bull Entomol Res* 1946 Feb \ 36 Pt 4 395-415 3 figs [13 refs.]

The experiments were carried out in a village near Freetown, Sierra Leone, and at Kرابonekrom near Sekondi, Gold Coast. The author throughout compares his findings in West Africa with those obtained by HADDOW [this *Bulletin* 1942 \ 39 595] in Kenya. All catches were made by collecting mosquitoes after spraying the room with a pyrethrum-in-kerosene mixture. In order to avoid any repellent effect, a series of identical huts were used and the human bait was shifted to a fresh house after each catch. Ribbards

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considers that if this precaution is used the spray method is more efficient than the hand-catching employed by Haddow.

In West Africa, female anophelines were virtually absent from unoccupied huts. The author suggests that the higher proportion found in such huts in Kenya may be the result of outdoor conditions which in East Africa may be less favourable to adult anophelines. The great majority of *A. gambiae* and *A. funestus* which have fed in native houses remain there until after dawn, the period which elapses after dawn before they finally leave the hut depends on the extent to which the interior of the hut is exposed to daylight. *A. melas* seldom left huts in which they had fed, if there was little light or ventilation until after dark the following day.

As suggested by the title of the paper Ribbands devoted considerable attention to the influence of moonlight on the house-haunting habits of West African anophelines, a subject which, so far as the reviewer is aware has previously received but little attention. The results obtained proved a high degree of correlation between the time of moonlight and the time of entry of *A. funestus* the figures for *A. gambiae* were inadequate, but the author suspects that a similar relationship probably exists. The following is quoted from that part of his summary concerned with the effects of moonlight: "During moonless periods, the fighting of ♀ *A. funestus* was partially inhibited, and when the moon came out, the waiting mosquitos entered the huts in greatest numbers. The average proportion caught when the moon rose during catching periods ending 10 p.m., midnight and 7 a.m. was approximately 50 per cent., 100 per cent. and 400 per cent. greater respectively than the proportion caught during these periods on moonless nights. On moonless nights many mosquitos waited until twilight of the following evening before entering the huts, and in consequence the average proportion caught in the period ending 8 p.m. was six times greater on moonless nights than on the nights after full moon.

"The records for ♀ *A. melas* are less complete and the correlation coefficient for the relation between time of entry and time of moonlight has the value of  $0.421 \pm 0.184$  a result which is barely significant. In view of the highly significant correlations found in the case of *A. funestus* it is unlikely that this correlation is fortuitous.

The author considers that in view of the high correlation which he has shown to exist between the time of moonlight and the time of fighting, it would be useless to compile records of the average time of entry into houses unless either the readings were sufficiently numerous to cancel out the effects of the lunar cycle or else weighted averages of percentage catches were used. With the latter method he obtained the following results:—

The average rate of entry of ♀ *A. funestus* throughout one complete lunar cycle at Krahonokrom Gold Coast, was 27 per cent. before 8 p.m., 22 between 8 p.m. and 10 p.m., 21 between 10 p.m. and midnight and 30 after midnight. The similar rates for *A. gambiae* (based on very few records) were 10, 20, 30 and 40 per cent. respectively. Comparable rates for *A. melas* in Sierra Leone are not available but at least 45 per cent. entered before 10 p.m. (=11 p.m. Gold Coast time).

As regards the time of feeding, Ribbands's observations show that in West Africa, anophelines usually rest on the wall of the hut for some little time before commencing their meal. Thus although 27 per cent. (figures based on *A. funestus*) of anophelines entered houses before 8 p.m., 58 per cent. of those caught at 8 p.m. were unfed whereas of the anophelines caught in huts after dawn, 95 per cent. were fully fed. The author points out that this may explain how residual DDT on walls is able to protect the occupants of the room against biting, since the mosquitoes are incapacitated during this preliminary short resting period.

[This is a most useful and interesting paper which should be consulted in the original by those concerned.]

GIVA A. Comportamento della citopoiesi midollare nei bambini malarici. [Cell Production in Bone Marrow of Malarious Children.] *Haematologica* Pavia. 1945 v 27 399-435 8 figs. [69 refs.] French summary  
R M Gordon

ECKSTEIN A & NIXON W C W Congenital Malaria. *Brit Med J* 1946 Mar 23 432-3

With wide experience of malaria in Turkey the authors contend that congenital malaria is not uncommon in places where the disease is endemic. They cite five cases [The ages of these infants ranged from 2 to 3 weeks so the possibility of infection after birth cannot be altogether excluded though this seems to have been unlikely in some cases] All five mothers were suffering from malaria. Three were *P vivax* infections two *P falciparum*. One of the infant patients was one of twins the other twin also harboured *P vivax* but presented no clinical signs of infection other than some enlargement of the spleen. It is suggested that high infant mortality rates might be reduced if mothers received adequate suppressive and prophylactic treatment during pregnancy  
Norman White

MAKARI J G The Cephalin Flocculation Test in Malaria. *Brit. Med J* 1946 Feb 23 272-3 2 figs

The cephalin-cholesterol flocculation test was first described by HANGER (*Trans Amer Phys* 1933 v 53 148) and has since proved its value as a test of hepatic function. The author applied it in 105 cases of malaria. A positive flocculation reaction was obtained in 96 cases (91.4 per cent.) in 94 of these the reaction was ++ or above. Both *P falciparum* and *P vivax* infections were included. The reaction tended to become negative with anti-malaria treatment. It is suggested that the test might be used on cerebro-spinal fluid in cerebral malaria to determine the degree of activity of the infection and that it might be used as a routine on prospective blood donors. Ninety persons in whom there was no evidence of either malaria or liver disease were also examined in all the cephalin flocculation test was negative.  
Norman White

JENYINGS G H. Coma as Onset in a Case of Malaria in England. [Memoranda.] *Brit Med J* 1946 Apr 27 650

The patient, a man aged 23 had lived in West Africa for 11 months during which he had taken 10 grains of quinine daily as a prophylactic [presumably effective] against malaria, but had discontinued taking it on leaving for England. A few days after his arrival in England he had had two very short attacks of fever and felt apathetic and rather sleepy during the following six weeks for a week before his admission to hospital he had been treated at his home for anaemia. He complained of pain in his right arm 24 hours before admission and on the evening of the next day coma with high fever (105°F) developed suddenly and he was admitted to hospital.

Condition on admission.—Temperature 104.2°F respiration 36 deep and noisy pupils moderately dilated not reacting to light no neck rigidity tendon jerks much exaggerated bilateral ankle clonus present plantar reflexes extensor abdominal reflexes absent spleen 3 inches below the ribs blood showed numerous subtertian malarial parasites.

**Course and treatment**—He was given quinine bishydrochloride 20 grains intravenously and, later tepid sponging his temperature fell and he quickly recovered consciousness. Next day he was bright and alert but very pale the spleen was undiminished in size the blood showed Hb 40 per cent. R.B.C. 1 720 000 C.I 1 17 W.B.C 3 260 (P 5 per cent., L 40 per cent. M 8 per cent.) He was given quinine bishydrochloride 10 grains t.i.d. and mepacrine 0.1 gm. t.i.d. for two days then quinine bishydrochloride 5 grains t.i.d. and ferri et ammon. cit. 40-90 grains daily. Six days after admission the spleen was no longer palpable and the abdominal reflexes were normal but the tendon jerks in the legs were still slightly exaggerated. After taking a 5-day course of pamaquim 0.02 gm. t.i.d. he was discharged on the 17th day after admission his blood then showed Hb. 70 per cent. R.B.C 3 660 000 C.I 0.92 W.B.C 6 400 (P 72 per cent. L 20 per cent. M 7 per cent. E 1 per cent.) His temperature became normal after the second day. Two months later he showed no anaemia and had had no relapses.

J F Corson

# PARRY E. Surgery in Malaria. *Lancet* 1946 Jan 12, 49-51

In many cases of *P. falciparum* infection there is a tendency to haemorrhage. Such haemorrhage can lead to mistakes in diagnosis. It was the outstanding characteristic of eight interesting surgical cases cited by the author in all of which the prompt recognition of a coexisting *P. falciparum* infection and the prompt intravenous administration of quinine were quickly followed by cessation of bleeding. The cases include a compound fracture of both bones of the leg a penetrating wound of the neck a fracture of the pelvis with rupture of the urethra profuse epistaxis two cases of haemorrhage into adenomata of the thyroid and a case of appendicitis in which numerous subserous petechial haemorrhages in visceral and parietal peritoneum were attributable to malaria infection. Malaria is liable to concentrate on the lungs after an inhalation anaesthesia just as it tends to cause cerebral malaria after intravenous anaesthesia.

The author states that to anyone who has been in the far-eastern theatre of war since its beginning the beneficial changes wrought by mepacrine in the treatment of malaria are little short of miraculous.

Norman White

# DOLE, V P & EMERSON, K Jr with the technical assistance of Esther BRAUN Electrophoretic Changes in the Plasma Protein Patterns of Patients with Relapsing Malaria. *J Clin Investigation* 1945 Sept v 24 No. 5 644-7 1 fig

The total protein, albumin and globulin content of the plasma of eight patients suffering from *P. vivax* malaria was measured during the clinical attack after the patients had been allowed three paroxysms, and at varying times subsequently. The albumin and globulin fractions were estimated by electrophoresis and by salt fractionation.

The authors found that during the malarial attack the total protein remained within normal limits. The albumin/globulin ratio was depressed. The increase in globulin occurred mainly in the fibrinogen and  $\gamma$  globulin fractions. The mobility of the protein was normal during the malarial attack. The plasma protein content returned to normal after specific treatment and during the inter-relapse period.

In a single case of *P. falciparum* malaria which was untreated for 3 weeks, the total protein dropped to 3.61 gm. per cent. (normal value 6.7) with an albumin globulin ratio of 1.3 (salt fractionation) or 0.72 (electrophoretic).—

The author considers that the changes in plasma protein are not specific in malaria. Consequently methods of diagnosis based on the protein pattern are not reliable in malaria [see PROSKE & WATSON this *Bulletin* 1939 v 36 813] particularly as the pattern returns to normal between relapses although the infection with *P. vivax* must persist during this period.

[The authors do not attempt to relate the protein pattern to the effects of treatment although their figures show that in one case treated with atabrine (mepacrine) the plasma protein reached a maximum concentration during treatment whereas in another case treated with quinine the protein was depressed during treatment and rose to a maximum after treatment was finished]

B G Macgregor

LE CHUITOV F La prophylaxie et le traitement du paludisme dans la marine  
[The Prophylaxis and Treatment of Malaria in the French Navy] *Bull Soc Path Exot* 1946 v 39 Nos 1/2, 36-43

SIMPSON J C E & SCHOFIELD R Antimalarial Action of Cinnoline Derivatives.  
[Correspondence] *Nature* 1946 Apr 6 439-40

KELSEY F E OLDHAM F R, CANTRELL W & GEILINO E M R. Antimalarial Activity and Toxicity of a Metabolic Derivative of Quinine. [Correspondence] *Nature* 1946 Apr 6 440

YUDEIN J Urinary Mepacrine in relation to Incidence and Diagnosis of Malaria. *Lancet* 1946 Mar 16 377-80 1 chart

This paper describes the results of estimation of urinary mepacrine in groups of healthy European Service personnel in W. Africa with different malarial incidence (all malignant tertian) and in unselected patients admitted to hospital there. All the subjects were supposed to be having 0.7 gm. of mepacrine weekly as a suppressive. For estimation the method of YUDEIN [this *Bulletin* 1945 v 42 863] was employed. Since there is a relationship between the amount of mepacrine excreted in the urine and its level in the blood, the amount of drug excreted in unit time might therefore be related to the incidence of malaria. As completely reliable 24-hour specimens of urine could not be obtained 8-hour specimens were used. It was found that the lowest excretion of drug occurred in the group of subjects with highest incidence of malaria. For practical reasons a method was developed in which random samples of urine were used for the estimation of mepacrine excretion. Output depends on concentration of drug as well as on the volume of urine passed, and the latter has an influence on the specific gravity of the sample. To estimate the output of mepacrine, its concentration in a random sample of urine was determined and also the specific gravity of the specimen. The concentration value for a urine of sp. gr. 1.010 was then calculated and the author terms this latter value—the standard urinary concentration of mepacrine. It was found that figures for the relative excretion of mepacrine in individuals or in groups were similar when estimated either as standard concentration or as total output over a period. The concentration of mepacrine was measured by the former method in 149 cases divided into four groups as follows—(1) proved malaria (2) clinical malaria (no parasites seen in blood but signs and symptoms suggestive) (3) other medical conditions (4) surgical conditions. In cases of proved malaria the excretion of mepacrine was found to be low. The author believes that a high excretion of mepacrine should exclude a diagnosis of malaria. From his own and other evidence he concludes that a

high proportion of cases diagnosed as clinical malaria are in fact not malaria. [This is in contrast to the experience of HYMAN (this Bulletin 1945 v 42, 937) in South Pacific Areas.]

J. D. FALLON

ELLERBROOK, L. D. LIPPINCOTT, S. W. CATEXO, C. F. GORDON, H. H. & MARBLE, A. Plasma Quinacrine Concentration in Treatment of *Plasmodium vivax* Malaria acquired in the South Pacific. *Arch. Intern. Med.* 1945 Nov-Dec. v 78 No 5 352-7 7 figs.

Mepacrine (quinacrine) was estimated by the method of BRODIE and UDENFRIEND (this Bulletin 1943 v 40 821). When known amounts were added to plasma, an average recovery of 98 per cent. (82-110 per cent.) was obtained. An average blank value of 3 micrograms per litre was observed in the plasma of untreated persons. Determinations were made on 6 733 specimens from 291 patients with relapsing malaria, treated in Texas. Doses were given with meals (at 7.30 a.m., 11.30 a.m. and 5 p.m.) and specimens for estimation were collected before breakfast. There were four groups of patients. Group I (54 patients) received 0.2 gm. orally at meals and at midnight for 5 doses and then 0.1 gm. thrice daily until a total of 2.8 gm. had been received. The plasma concentration in this group is shown in Fig. 1 in which the heavy line represents the average for the group and the two lighter lines indicate 1 standard deviation on each side of the mean (and include approximately 2/3 of all values). Patients in Group II received 2.8 gm. of mepacrine on 8 days of the week until the sixteenth day from the start of treatment. Group III was similar but the pamaquin was omitted. The plasma levels in these two groups were similar to those of Group I except that after the 14th day an approximately steady level of plasma mepacrine was maintained at 20-30 micrograms per litre. The average diurnal variation is shown in Fig. 2. In Group IV 0.4 gm. of mepacrine was given at 9 a.m. followed by 0.2 gm. at 4.30 p.m. and at 1 a.m. then 0.2 gm. was given at 9 a.m. and 9 p.m. for 6

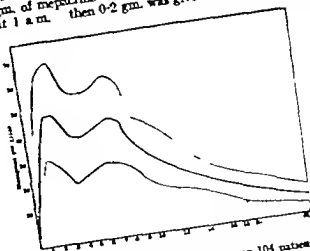


Fig. 1.—Fasting plasma quinacrine concentrations in 104 patients for eight days and in 54 patients thereafter (2.8 Gm. of quinacrine hydrochloride in one week). The heavy line indicates average values. In Figs. 1 and 4 fine lines indicate 1 standard deviation (includes approximately two-thirds of all values).

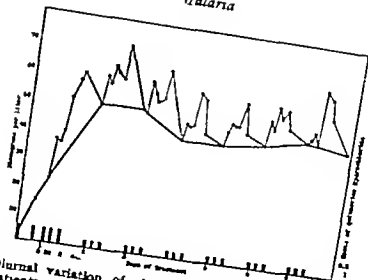


Fig 2—Diurnal variation of plasma quinacrine concentrations in 104 patients given 28 Gm of quinacrine hydrochloride

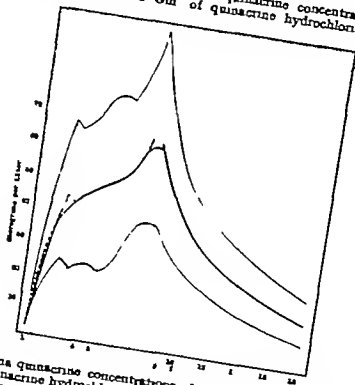


Fig 4—Plasma quinacrine concentrations of 35 patients who were given 32 Gm of quinacrine hydrochloride in one week. The heavy line indicates average fasting values. The broken line indicates five hours after administration of 0.2 Gm.

[Reproduced from the *Archives of Internal Medicine*]

days. The average plasma concentration of mepacrine is shown in Fig 4. Under these treatments pyrexia and other symptoms rapidly subsided and parasites disappeared from the blood.

ABBEY E. A. & LAWRENCE E. A. The Effect of Atabrine Suppressive Therapy on Eyesight in Pilots. *J Amer Med Ass* 1946 Mar 23; 130 No. 12, 786-7

1 The continued use of atabrine in doses of one tablet (0.1 Gm.) a day appears to have no effect on visual acuity except in a highly sensitive and rare individual.

to be related to natural and acquired immunity which would be modified by the destruction of lymphocytes which irradiation brings about.

C. M. Wernon

RIGDON, R. H. & VARRADOR, NORA B. Transfusions of Red Cells in Malaria. An Experimental Study in Ducks. *Amer J Trop Med* 1945 Sept \ 25 No 5 409-15 5 figs [11 refs]

In young ducks *Plasmodium lophoceres* infections usually terminate fatally with low counts of both the red blood corpuscles and parasites. The parasites increase during the course of about a week to reach a peak in which the blood shows from 355 to 490 infected cells for 500 red cells. Shortly before the peak is reached the number of red cells begins to diminish rapidly to fall in the course of 48 hours to 500 000 per cmm. From 2 to 24 hours after the commencement of the fall in the red cells the diminution in the number of parasites begins. Not infrequently following the commencement of the fall in the parasite count there is a short rise in the count which does not usually reach the initial peak. In the case of the occasional duck that survives the parasites disappear from the blood while there is a rapid increase in the red cell count, which reaches normal in about a week. If infected ducks are transfused with normal duck blood in sufficient amounts to maintain the red cell count at its normal level it is found that the parasite count also remains high. The transfusion thus not only postpones the advent of the anaemia but also delays the fall in the parasite count. This result is reached only if the quantity of normal blood is adequate e.g. 5 transfusions of 5 cc. and 4 of 10 cc. in 48 hours. If the quantity is less than this the course of the infection is unaffected. Though transfusion may not save the life of the ducks its immediate effect is a marked improvement in health which is most evident in the most anaemic. It is generally supposed that phagocytosis is mainly responsible for the fall in the parasite count which occurs after the peak has been reached. The authors consider that if this were true the parasite count should not be maintained by transfusion which would not be expected to prevent phagocytosis from progressing normally. They suggest that factors other than phagocytosis may be significant in producing the decrease in the parasite count which follows the peak of the infection.

C. M. Wernon

TALIAFERRO, W. H. & BLOOM, W. Inflammatory Reactions in the Skin of Normal and Immune Canaries and Monkeys after the Local Injection of Malarial Blood. *J Infect Dis.* 1945 Sept-Oct \ 77 No 2, 109-38, 7 pls [25 refs]

The object of the experiments described in this paper was the study of the local reactions when small quantities of malarial blood were inoculated subcutaneously (canaries) or intracutaneously (monkeys) into normal and immune canaries and monkeys. The malarial parasites involved were *P. cathemerium* for the canaries, *P. brasilianum* for cebus and spider monkeys, and *P. knowlesi* for rhesus monkeys. Control experiments were carried out by injecting normal blood or trypan blue. Conclusive evidence was obtained that the reaction was much more marked with *P. knowlesi* than with the other parasites. Thus red cells containing large stages of *P. knowlesi* were agglutinated and localized in the skin of immune rhesus monkeys but were not agglutinated at all in normal rhesus monkeys. In addition, inflammation including phagocytosis by heterophiles\* and macrophages was more marked in the skin of immune than of

\*Heterophile leucocytes in man and in the above species of monkeys are the polymorphonuclear neutrophils; the granules are more acidophilic in the guinea-pig, rabbit and canary and were called pseudo-eosinophils. See MAXIMOW & BLOOM, "Textbook of Histology" 1942, 4th Ed. Saunders, pp. 47 & 48.—Editor

normal rhesus monkeys. In contrast inflammation was less marked in immune canaries, cebus monkeys and spider monkeys while agglutination did not occur. It would seem that the marked reaction in immune rhesus monkeys is due to the great content of circulating antibody which allows effective amounts of this substance to leave the blood and enter the inflamed area. In both immune and non-immune monkeys and canaries skin reactions to injections of malarial blood or trypan blue proceeded more rapidly than do the reactions in the skin of rats following the injection of trypan blue as described by the MÖLLENDORFFS and MAXIMOW.

C. M. Wenyon

KNISELY, M. H., ELIOT, T. S. & BLOCH, E. H. Sludged Blood in Traumatic Shock. I. Microscopic Observations of the Precipitation and Agglutination of Blood flowing through Vessels in Crushed Tissues. *Arch. Surg.* 1945 Nov-Dec v 51 No 4 220-36 1 fig [Refs in footnotes]

\* This paper contains a further report on the direct microscopic examination of blood and small vessels in living frogs and mammals under normal conditions and following damage by crushing and also in stage III of acute *P. knowlesi* malaria in monkeys: see also this *Bulletin* 1943 v 40 534].

Under control conditions the authors observed that circulating red cells travel free inside the vessels and do not agglutinate and that white cells do not stick to the vessel endothelium.

In stage III of *P. knowlesi* infection a thick glassy precipitate forms between and around the red cells: the precipitate forming simultaneously in about 20 minutes throughout the whole body. The precipitate binds the cells together in wads and masses (*not rouleaux*): the circulating blood coming to resemble sludge. This sludge resists its own flow through the small vessels so that stagnant anoxia develops: the affected endothelium ultimately allowing fluid to leak into the tissues with steady loss of intravascular fluid volume. Anoxia of the endothelium alone is sufficient to cause this. The red cells in *P. knowlesi* infection are not stuck to the endothelium but are apparently stuck to the phagocytes of the liver, bone marrow and spleen, which readily ingest them, so contributing towards the malarial anaemia.

The authors consider the precipitate to be fibrin or something similar to it, and devised experiments to observe the effect of the introduction of freshly formed fibrin into the circulation. For this purpose they observed the behaviour of blood cells and vessels in living animals after crushing trauma of various degrees: first in the omentum and then in muscle. They found that after crushing there were in general, three regions of injury —

(a) A zone in which small vessels are thrombosed: no sludge is poured into the venous system.

(b) A sludging zone in which each venule pours out sludge into the general circulation: such out pouring going on for long periods.

(c) A zone in which there is insufficient injury to cause any detectable change in the circulating blood.

The authors conclude that when they are crushed striated and smooth muscles release substances capable of diffusing in through the vessel walls and reacting with constituents of the blood flowing through the patent vessels.

[This important paper should be read in the original by those who are interested in the vascular phenomena associated with shock like conditions]

B. G. Macgregor.



to be related to natural and acquired immunity which would be modified by the destruction of lymphocytes which irradiation brings about.

C M Wenyon

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\*Heterophile leucocytes in man and in the above species of monkeys are the polymorphonuclear neutrophils; the granules are more acidophilic in the guinea-pig, rabbit and canary and were called pseudo-eosinophile. See Minton & Bloom, "Textbook of Histology" 1942, 4th Ed. Saunders, pp. 47 & 48.—Editor

[The arguments in this paper are facile but not altogether convincing in some respects. Nevertheless it is a valuable paper the importance of which is perhaps best expressed in the words of Schwenker and Comptoir (1939 referred to by Dr Gear) the entire theory discussed here is based on only a frail foundation. However what evidence there is supports it as a possibility. Its value lies in offering a basis for further experimental work.]

B G Macgrath

SINGH I & SINGH I A Further Note on the Treatment of Black Water Fever with Antivenene *J Indian Med Ass* 1946 Feb v 15 No 5 147-8

## TRYPANOSOMIASIS

GALLAIS P Les formes neuro-psychiques de la trypanosomiase humaine africaine (Essai d'une systématisation clinique et physiopathologique) [The Neuropsychological Forms of African Human Trypanosomiasis.] *Les Grandes Endémies Tropicales* (Onzième Année.) 1939 Paris pp 113-51

The symptoms and signs of African sleeping sickness are all well known but they have not yet been systematically grouped and the author thinks that this explains why physicians outside tropical Africa often fail to diagnose the disease. In the nervous stage there is a general family resemblance among sleeping sickness patients. The disease is a diffuse meningo-encephalitis which though it resembles syphilitic meningo-encephalitis to some extent has special features of its own. Certain regions of the central nervous system are particularly affected and this gives it a clinical picture very different from that of general paralysis.

The fundamental neuro-psychical syndrome results from involvement of the region around the third ventricle—the hypothalamic region with the nuclei of the autonomous nervous system which are situated there. The symptoms may be classified as tropho-vegetative, psychic, motor and sensory. These are described in considerable detail with notes of illustrative cases.

The author discusses the pathological lesions of the central nervous system they are associated with the capillaries and the Virchow Robin perivascular sheaths. He concludes that in trypanosomiasis there is a diffuse involvement of the walls of the cavities—the pia-arachnoid membrane with its prolongations and the ventricular ependyma with the choroid plexuses i.e. the parts where the cerebrospinal fluid is formed, circulates and is reabsorbed.

J F Corson

BROWNING C H, CALVER, K. M, LECKIE M W & WALLS L. P Phenanthridine Compounds as Chemotherapeutic Agents in Experimental *T. cruzi* Infections. [Correspondence.] *Nature* 1946 Mar 2 263-4

Prior to the present report there was only one compound known to exercise a favourable influence on *T. cruzi* infections, namely Bayer 7602 (Ac). [The reviewer has been informed by Dr F H S. Curd of Imperial Chemical Industries Ltd. that previously published descriptions of the constitution of this compound repeated in the article under review are incomplete or incorrect. The true formula has now been published by H.M. Stationery Office in British Intelligence Objectives Sub-Committee (BIOS) Final Report No 116 Item No 24. Pharmaceuticals Research and Manufacture at I.G. Farbenindustrie page 53. It is diallylmalondi (4-amino-2-methyl-quinolyl-1-6-amide).]

## BLACKWATER FEVER.

GRAB J. Autoantigens and Autoantibodies in the Pathogenesis of Disease with special reference to Blackwater Fever. *Trans. Roy Soc Trop Med & Hyg* 1946 Feb v 39 No. 4, 301-14. [24 refs.]

The author states that in previous unpublished experiments he found that, whereas an emulsion of homologous liver produced no liver-antibodies when injected into rhesus monkeys (whether normal or protected by vaccine against yellow fever) an emulsion of liver from a rhesus monkey dead of yellow fever produced liver antibodies after injection into a rhesus monkey protected by vaccine against yellow fever. These results are similar to those obtained by SCHWETTER and COMPTONER (*J Exper Med* 1939 v 70 223) who reported the production of complement fixing antibodies reacting with both rabbit kidney and brain following the injection of emulsions of homologous kidney plus staphylococcal or streptococcal toxins into the rabbit.

On the strength of these observations the author suggests that the lysis of red cells in blackwater fever may result from the action of an autolysin produced in the following manner —

- |   |                   |
|---|-------------------|
| i. Red cell + malaria parasite  | } = auto-antigen. |
| or " " - - - - - antimalarial drug  |                   |
| or " " - - - - - antimalarial drug  |                   |
| ii. Auto-antigen + reticulo-endothelial system = auto-antibody (haemolysin) |                   |
| iii. Red cell + haemolysin = sensitized red cell.                           |                   |
| iv. Sensitized red cell + complement = lysis.                               |                   |

The theory is best expressed in the author's own words —

Red cells infected with malarial parasites, possibly only after treatment with an antimalarial drug or red cells altered by or combined with an antimalarial drug become autoantigenic and in response to this autoantigen an antibody or haemolysin is produced by the reticulo-endothelial system, particularly by the spleen. The titre of this haemolysin is boosted by each repeat attack of malaria. When the circulation of the blood through the spleen is free this haemolysin is mopped up by the red cells and these sensitized red cells are removed by the reticulo-endothelial cells as they are sensitized and before a demonstrable intravascular haemolysis occurs. However when the circulation through the spleen is impeded and the spleen becomes congested, as it does in an attack of malaria, which also provides a secondary stimulus to boost the titre this haemolysin accumulates. Factors which cause a sudden contraction of the spleen such as the administration of quinine (*sic*), chill, and exertion now would suddenly express into the general circulation sufficient haemolysin to sensitize a large number of red cells and their haemolysis intravascularly would result in haemoglobinæmia and haemoglobinuria followed by the other signs and symptoms of blackwater fever.

The relevant literature on blackwater fever is reviewed. Points which the author considers to be in favour of his hypothesis are —

(a) The occurrence of erythrophagocytosis, autoagglutination and spherocytosis in blackwater fever (all suggesting the presence of antibodies)

(b) The experiments of FOR *et al.* [*this Bulletin* 1942 v 39 206 1945 v 42, 634] in which it was found that normal red cells injected into blackwater fever circulation and, conversely red cells from an actively haemolyzing blackwater fever patient injected into a normal circulation were rapidly destroyed.

(c) The analogous effects produced by artificial lytic sera.

(d) The time lag between the first attack of malaria and the onset of blackwater fever which suggests a process of sensitization.

commenced with an initial dose of 0.2 to 0.5 cc. according to the age and weight of the child this was increased till a maximum daily dose was reached which varied from 0.7 to 2 cc. Thus in a child 4 years old weighing 14.5 kilo the course consisted of 0.5 1.0 1.5 followed by nine doses of 2.0 cc.

C. M. H. Enyon

## FEVERS OF THE TYPHUS GROUP

OLITZKI L. OLEINIK, E. CZACIKES J. W. & HUTZENOK A. Thermostable Endotoxin of *Rickettsiae*. [Correspondence] *Nature* 1946 Apr 27 552.

GROUPÉ V & DONOVICK R. Studies on Toxicity Complement-Fixing and Immunogenic Activity of Typhus-Infected Yolk Sacs. *Proc Soc Exper Biol & Med* 1945 Dec 1 60 No 3 349-51 [10 refs.]

In the conditions described in the paper it was found that suspensions of yolk sacs infected with the Breinl strain of epidemic-typhus rickettsiae increased in toxicity in relation to the number of days of survival of the chick embryos from which the suspensions were prepared. Vaccines prepared from the suspensions showed a corresponding rise in antigenicity in relation to the survival period and the complement fixing activity of the antigens contained in the vaccines increased in the same way.

The toxicity experiments were carried out with untreated yolk-sac suspensions prepared from embryos still living on the 5th 6th 7th and 8th days respectively after inoculation and it was found that certain dilutions of the 5th-day suspensions failed to kill any of the test mice whereas corresponding dilutions of 8th-day suspensions killed all the test mice. The complement fixing titres of these suspensions showed a corresponding degree of variation being lowest in 5th-day suspensions and highest in 8th-day suspensions.

Vaccines were prepared from yolk sacs of embryos that died 5-7 days after inoculation and from yolk sacs of embryos still surviving after 7 days the results of tests of these vaccines are illustrated by the following examples —

	Vaccines prepared from embryos			
	D-5 <sup>(1)</sup>	D-6	D-7	L-7 <sup>(2)</sup>
Number of yolk sacs	90	102	146	65
Richness in rickettsiae	±	+	++	+++±
Complement fixation at titre 1-64	0	2+	3+	4+
Percentage of mice protected by 0.2 ml. of vaccine	21.4	62.9	No test	85.7

(1) D-5 means dead after 5 days. (2) L-7 means still alive after 7 days.

The toxic and complement-fixing substances are not identical the former are destroyed by formal and ether which do not affect the latter yet both are more active in yolk-sac suspensions of long-surviving than of short-surviving embryos.

John W. D. Megaw

DONOVICK R. FARRELL Mary & SMITH Florence. The Antibody Response of Guinea Pigs to Epidemic Typhus Vaccines of various Antigenicities. *J Bacteriology* 1945 Sept 50 No 3 241-7 3 figs

In this investigation 48 lots each consisting of 12-20 guinea-pigs were vaccinated with two doses of one of 43 different batches of epidemic typhus

[July 1946]

The authors found that a number of phenanthridine compounds exhibit definite therapeutic activity against these infections in mice. In order to examine the matter properly it was first necessary to determine accurately the course of untreated *T. cruzi* mouse infections, since these tend to be somewhat variable. The authors therefore passaged their strain, subcutaneously as soon as parasites became numerous in the blood since previous work with *T. congolense* had shown the advantages of using such an "acme" strain [BROWN and CALVER, this Bulletin 1945 v. 42, 259]. CALVER, *ibid.* 704]. In more than 140 such passages the trypanosomes became abundant in the blood in all but one case and 82 per cent. of the mice died of the infection within 30 days, mostly between the thirteenth and nineteenth days. The remaining 18 per cent. showed a chronic course, surviving indefinitely, and parasites were scanty or absent for prolonged periods. Accordingly in assessing the effect of treatment it was necessary to allow for spontaneous suppression of the infection in a proportion equivalent to that shown by untreated controls.

Treatment consisted of one subcutaneous injection given as soon as scanty parasites appeared in the blood, and mice were reckoned as cured if trypanosomes disappeared from the blood permanently, either at once or after becoming numerous for not more than two or three days. The question of possible influence on the intracellular stage of the parasite was not examined. Activity similar to that exhibited by Bayer 7802 (Ac) was shown by 3-carbethoxyrhamno-9- $\beta$ -carbethoxyrhamno-10-methylphenanthridinium chloride (S 1544) and the corresponding much more soluble, methanesulphonate (S 1577). The degree of activity, although the best yet encountered, is still not of a very high order.

It is interesting that the presence of a phenyl ring in the 9 position is not essential for activity as was shown by a significant therapeutic response to 2,7-dicarbethoxyrhamno-9-10-dimethylphenanthridinium methanesulphonate (S 1582).

Immunity phenomena were believed to play a considerable part in the therapeutic effect since cured animals and those showing suppression of infection failed to develop an obvious infection when reinoculated, even many months later. Nevertheless, unlike the case with *T. congolense* [BROWN and CALVER, *loc. cit.*] treatment is more successful at an early stage of infection than later when parasites are numerous in the blood. The above phenanthridinium compounds which influence *T. cruzi* do not affect *T. brucei* or *T. congolense* infections, except in high doses. E. V. LOMAX.

### LEISHMANIASIS.

MORALES A. L. Nueva aportacion a la quimioterapia del Kala Azar infantil por el Solusibosol concentrado. "Treatment of Infantile Kala Azar with Concentrated Solusibosol." *Rev. Sanidad Hig. Publica.* 1945 Aug., v. 19, no. 8, 529-35.

The paper reports the successful treatment of ten cases of infantile kala azar in children up to five years of age, with concentrated solusibosol (sodium antimony gluconate). The drug was given intramuscularly in ten or eleven daily doses. In three cases the total quantity was 1 cc. per kilo. of body weight in seven it was 1.5 cc. Better and more rapid results were obtained with the higher dosage, which was well tolerated by all the children. Treatment

commented with an initial dose of 0.2 to 0.5 cc. according to the age and weight of the child this was increased till a maximum daily dose was reached which varied from 0.7 to 2 cc. Thus in a child 4 years old weighing 14.5 kilo the course consisted of 0.5 1.0 1.5 followed by nine doses of 2.0 cc.

C. M. Henson

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In this investigation 48 lots, each consisting of 12-20 guineapigs, were vaccinated with two doses of one of 43 different batches of epidemic typhus

[July 1946]

vaccine, the sera of each lot of animals were collected and pooled 14 days after the administration of the second dose of vaccine. The antigenic titres of the vaccines ranged from 1-8 to 1-32. The antibody titres of the sera were tested by complement-fixation and mouse-neutralizing tests, and were found to correspond broadly with each other and also with the antigenic titre of vaccines employed in immunizing the animals.

The authors conclude that a direct determination of the antigenic titre of the vaccine by the complement-fixation test appears to give an accurate measure of its protective value for guinea-pigs.

The general trend of the findings can be seen from the following analysis of the tables contained in the paper —

Antigenic Titre of Vaccine		Antibody Titres of Sera of Pools of 12-20 Vaccinated Guinea-pigs			Mouse-Neutralizing Titres		
		Complement Fixation Titres			Range		
		Range	1-8 or less	1-16 or more	1-8 or less	1-16 or more	1-32 or more
1-8	13	1-4 to 1-32	5	6	1-8 to 1-32	4	6
1-16	19	1-4 to 1-128	6	8	1-8 to 1-128	6	5
1-32	16	1-8 to 1-256	1	4	1-8 to 1-64	2	4

Surprisingly great variations were observed in the antibody titres of different lots of animals immunized by the same vaccines. In some cases the complement fixation titres ranged from 1-8 to 1-32, and in one case the mouse-neutralizing titre of pooled serum from one lot of 20 guinea-pigs was 1-128 whereas the titre of another lot of 20 that had received the same vaccine was 1-8. Even allowing for great variations in the susceptibility of individual animals it would not be expected that two lots of pooled serum, each obtained from 20 guinea-pigs selected at random and treated in the same way should show such differences in their responses. The author feels compelled to suggest that it would be necessary to include 100 or more animals in each lot in order to obtain approximately similar responses with the pooled sera. John W. D. McGraw

DE ALBERTI, E. Epidemia di tifo esantematico in Grecia [An Epidemic of Typhus in Greece.] *Giorn. di Batteriol. e Immunol.* 1943 Aug v 31 No 2 89-98 English summary (4 lines)

YEOMANS, A. SNYDER, J. C. MURRAY, E. S. ECKE, R. S. & ZARAFONETIS, C. J. D. Anemia in Typhus Fever. *Ann Intern Med.* 1945 Nov v 23 No 5 711-53 10 charts (38 refs)

The authors comment on the scantiness of the information available on the subject of anaemia in the literature of typhus fever and on the greatly conflicting views expressed by the few German and French workers who have studied the condition.

In the present investigation, 64 Egyptian patients were studied in the U.S.A. Typhus-Compassion Ward of the Cairo Fever Hospital in 1943-44. It was soon found that the severest cases were in a condition of anaemia which was regarded as existing when the non-protein nitrogen of the blood was

45 mgm or over per 100 cc. Some of the patients affected were in a uraemic condition some had pronounced hypotension and some were severely dehydrated

The incidence and degree of azotaemia among the patients is shown in the table which has been compiled from data contained in the paper —

Severity of attack	No of patients	No. having azotaemia	Maximum Non Protein Nitrogen in Blood of Azotaemic Patients (mgm. per 100 cc.)	
			Average	Range
Very mild	2	0	—	—
Moderate	14	4	58	47-74
Severe	26	9	69	58-117
Very Severe	7	5	92	72-162
Fatal	15	15	120	75-200

The average age of the 64 patients was 28 years of the 15 who died it was 33 years. There were no deaths among the patients who remained free from the condition. The average daily blood pressure was not lowered in the affected patients but in many cases there was a sudden fall in the systolic pressure at the time of onset of the condition there was often also a diminution in the urinary output at this time azotaemia was rarely seen so long as the output remained above 2 000 cc. The time of onset was usually during the second week but in a few cases it was before the 8th day. The specific gravity of the urine tended to be low considering the reduction in the output. Dehydration often associated with insufficient fluid intake was regarded as an important contributory factor.

Albuminuria was present in all the cases red and white cells were often found in the urinary sediment cell casts were rarely seen but granular casts were often present. After recovery it was exceptional to find evidence of renal damage this occurred in two cases, but the kidneys might have been affected before the attack.

Detailed reports illustrated by charts are given of ten cases of which six were fatal. The investigation was exceptionally thorough and the charts form a graphic record of the chief features of each case.

The cause of the condition is discussed at some length. In view of the above reference to deficient fluid intake and of the statement that inadequate intake of total calories is an important contributory factor it is surprising to learn that the diet of most of the patients consisted of water sweetened fruit juices and 600 to 1,000 cc. of milk daily. [This diet which is inadequate in proteins as well as in calories (as the authors themselves state) would not be expected to support the nutrition of the renal cells the cardiac muscle, and the other tissues, already damaged by the infection. From the charts it appears that the daily fluid intake sometimes fell as low as two pints or even less. These circumstances combined with the high virulence of the infection and the relatively low standard of nutrition of the patients before the illness, may account for the exceptional degree of frequency of the condition in the present series of cases. Other observers have recorded very different findings for example, SCHÄFER (this Bulletin 1846 v 43 210) found no reading higher than 63 mgm. per 100 cc. during the second week among seven severe cases and in the two of these that were fatal the readings were 21 and 35 mgm respectively.]

John W D Meyer



[July 1946]

CRAUFORD-BENSON H J & MACLEOD J A.L.S., the Original British Army  
Louse Powder J Hygiene 1946 Jan., v 44 No 4 294-306 3 figs.  
[11 refs.]

This paper describes the work which led to the development of A.L.63 which was the official British Army louse powder from 1940 until the introduction of DDT in 1944. It was the only louse powder used by the British troops and the civilians employed by the British Army during the Naples typhus epidemic of 1943-44. Except for two cases, where negligence was shown, there were no cases of typhus among the troops or among the 25,000 civilian employees treated at fortnightly intervals.

The problem was to develop a preparation for use by the individual which would (a) kill lice already present (b) prevent infestation or re-infestation. The value of a preparation was established by laboratory scale tests, in which the lice were dusted and exposed to treated flannelette in boiling silk bottomed boxes worn on the leg during the daytime and by practical tests with naturally lousy people in a specially established clinic in the East End of London. In the latter experiments the underclothes or specially provided shirts worn next to the skin were dusted.

All the dusts were made up with a kerosin base. The substances tested included among others pyrethrum, derris, naphthalene, high boiling tar acids and creosote used alone and in various combinations. It was soon found that different results were obtained in the laboratory and field tests, and that, in general, higher concentrations of insecticide were necessary in the practical work.

Naphthalene killed the body lice most quickly but failed to give lasting protection. Derris and pyrethrum were toxic to lice, but either alone or mixed they were inferior to other insecticidal combinations. It was found that mixtures of high boiling tar acids and derris showed an activation effect and such a mixture was more effective than either ingredient alone. Thus activated derris mixture was slow in action, but gave better lasting protection than other mixtures. By combining the rapid action of naphthalene with the lasting effect of derris activated with high boiling tar acids, formula A.L.63 was obtained, i.e. high boiling tar acids, 2 per cent; derris root 14.3 per cent., giving 1 per cent rotenone; naphthalene 50.0 per cent; china clay 33.7 per cent. A.L.63 gave a 98 per cent kill of lice present on treated garments at the time of application and protection from reinfestation for five days. When the subject was exposed in an infested environment it was found that retreatment at eight-day intervals gave effective protection. Applied as a prophylactic to clean garment A.L.63 remained effective for seven to eight days and gave partial protection up to 16 days.

W A L. David.

CRAUFORD-BENSON H J Naples Typhus Epidemic, 1943-8 (as seen by an Entomologist Brit Med J 1946 Apr 13 578-80 1 graph.)

The epidemic of typhus in Naples during the winter of 1942-43 reached its maximum (900 cases a week) early in January and then the number of cases fell rapidly. Previous experience would have led to the expectation that the number of cases would have gone on increasing to much higher levels during the early months of 1943 and there is little doubt that a dramatic result was obtained by the control measures described in this paper. These consisted of the mechanical application of louse powders to fully clothed individuals, a method which though not immediately rendering them louse-free enabled enormous numbers to be dealt with (2,759,000 individual applications up to April 1943). It also made those treated relatively "louse-proof". Although

DDT is usually credited with the responsibility for the success achieved, it is here shown that the initial fall in incidence was mainly caused by the use of MYL the American powder containing pyrethrum and that the 20 000 civilian employees of the army were well protected by fortnightly dusting with the original powder AL63 which contains derris and naphthalene. The later control was by means of DDT

Kenneth Mellanby

WHEELER C M Control of Typhus in Italy 1943-1944 by Use of DDT *Amer J Pub Health* 1946 Feb 36 No 2 119-29

The author a member of the U.S.A. Typhus Commission describes the organization by which louse borne typhus was promptly brought under control in Naples and Southern Italy in 1943-44. The remarkable success which was achieved in Naples ceases to be a matter of surprise to anyone who reads this report.

Preventive measures were started under the direction of the medical staffs of the Allied Forces and later were controlled by the U.S.A. Typhus Commission. As is shown by the title of the paper chief reliance was placed on the use of DDT. This was used in the form of a 10 per cent dusting powder of which 1-1½ oz. was applied by hand-duster or by power-dusters to each person. The powder was blown between the skin and the inner layer of clothing and between the outer layers of clothing bedding and spare clothing in houses were also dusted when necessary.

The large team of workers employed was divided into a number of sections (1) Case Finding Section (2) Contact Delousing Section (3) Case Contact Service (4) Special Services (5) Recovery (Air Raid Shelter) Service (6) Mass-Delousing Section (7) Immunization Section (8) Flying Squadron Section later (9) a Refugee Section was established to deal with groups of refugees from Yugoslavia and other countries. The Flying Squadron Section attended to outbreaks reported from places outside Naples in southern Italy.

No adequate summary can be given of the work of the organization especially as this was modified from time to time according to the needs of the situation. In a table it is shown that in Naples more than two and a half million dusting operations were performed and in other places there were more than 600 000. The number of cases of typhus reported in Naples was 1 404 elsewhere in southern Italy there were 510 cases.

Within a month of the institution of control measures in Naples on December 15th 1943 a sharp decline in the number of cases set in and by February 20th 1944 the epidemic appeared to have been definitely broken.

The Mass-Delousing Section was organized for the primary purpose of delousing the entire civilian population of Naples. It was planned on the basis of 50 stations equipped to dust as many as 100 000 persons daily. By February 8th 40 such stations were working with a combined staff of 439 persons. The whole operation was a triumphant success not only for DDT but also for the persons who planned and conducted the campaign.

John W D Megaw

BEALL J C Permanent Program for Typhus Fever Control in Memphis, Tennessee. *Amer J Pub Health* 1946 Feb 36 No 2 161-8.

Readers outside the U.S.A. will probably be surprised to find that the Programme for Typhus-Fever Control described in this paper is purely one of rat control. The disease referred to is of course the one commonly called murine or endemic typhus not louse borne typhus.

[July 1946]

In Memphis City a permanent organization has been set up with a view to preventing the disease from establishing itself and apparently no cases had been reported till some months after the commencement of the planning of the campaign when an outbreak of six cases occurred in a feed mill during August and September 1943.

In the month of November of the same year the City Commissioners adopted an ordinance by which owners of all business premises were made responsible for keeping their buildings free from rats. The official organization included the purchase of initial equipment costing \$8,000 but it was planned on a self supporting basis and all owners were compelled to pay for the cost of the necessary operations whether these were carried out by themselves or by the special section of the health staff. The personnel of the organization consisted of a public-health engineer, three field foremen, a sanitarian, and 22 negro labourers of whom 12 were assigned to rat proofing, 8 to rat trapping and poisoning, and 2 to special work. Three 1½-ton trucks and one ½-ton truck. Up to the time of writing 299 business establishments had been dealt with at an average cost of \$47.76 each. Apart from the compulsory powers provided by the ordinance efforts were made to secure the willing co-operation of owners by a publicity campaign.

The residential area of the City has not yet come within the scope of the campaign, but plans are being made for the inclusion of these at a later date and for the compulsory inclusion of all new buildings.

The description of the organization will be found interesting by all concerned with rat control though so high a standard of achievement would be unattainable in most of the places where the rat is a menace to public health.

John W. D. McGee

JOHNSON D. H. & WHARTON G. W. Tsutsugamushi Disease. Epidemiology and Methods of Survey and Control. *U.S. Nat. Med. Bull.* 1946 Mar. 48 No. 3 459-72, 1 fig.

This paper contains a useful summary of what is known of the epidemiology and prevention of tsutsugamushi disease. The word chiggers is defined as "the larvae of mites of the family trombiculidae of which about 150 species are known including at least 100 in the regions in which the disease occurs. A description is given of the characteristics by which these larvae can be distinguished from other minute arthropods. Rickettsiae are believed to be introduced into the body of the host with the saliva, which is injected by the larvae and which dissolves the tissues, so preparing them for ingestion. The larva after its one and only meal, drops off and buries itself in the upper layers of the soil in the nymphal and adult stages and the mite is non-parasitic feeding on any object that disturbs their habitat. They are hatched out their swarm actively in the soil. When the larvae are hatched out they are transmitted through successive generations of mites. Infection is believed to be the real reservoir of infection. But even if the mites which may therefore be the real reservoirs of infection. But even if the animal hosts should be found to play no direct part in the transmission cycle they would still be essential for the maintenance of the mite population. Many vertebrates are often bitten and these when they migrate are likely to convey living birds are often bitten. Many rats make their nests in places suitable as habitats for the mites. The infected areas, which may be strictly localized, are usually moist, but well-drained, and are covered with herbaceous and scrubby vegetation. Such areas are specially likely to be selected as sites for camps. Coconut and other food

trees or plants attract rats. Water-logged or dry soil and dense jungle are seldom infested by mites

Directions are given for the trapping of rats and for the examination of these and the other vertebrate hosts for the detection of mites. Methods of protecting investigators from infection include the immediate immersion of trapped rats in 80 per cent alcohol ideally or alternatively the temporary use of tight lidded canisters the wearing of impregnated clothing frequent application to the hands and wrists of dimethyl phthalate and the placing of the dead bodies of animals under examination on large trays smeared with dimethyl phthalate

White porcelain cups were found suitable for collecting larvae the cups were placed on the ground in contact with the surface litter for one to five minutes and then examined.

If larvae are found on small mammals the presence of infection should be suspected abundant larvae on birds and reptiles are likely to be pest jiggers [larvae which cause scrub itch] Identification of species is a matter for experts.

Soil can be disinfested by DDT five to ten pounds of a 10 per cent powder is enough for each acre Dimethyl phthalate is used for personal protection and also for spraying the floors of tents and huts when the slower action of DDT might not be adequate Instructions are given for the impregnation of clothing and blankets with dimethyl phthalate which remains effective for two weeks in the absence of repeated wetting by rain. Untreated shorts should be worn under the impregnated outer garments to avoid irritation of the genitalia. For the protection of one person two ounces of dimethyl phthalate can be applied by the smear method in which a few drops at a time are spread on the palms of the hands and rubbed on the socks and clothing by repeated applications till the whole surface has been uniformly treated

The exposed skin is also smeared lightly avoiding the lips and eyes.

Dibutyl phthalate used by the smear method is preferred by the Australian Army its effect is slower but is said to be more persistent

Rat control by trapping and poisoning is recommended [though in view of the authors own account of the life-history of the mites the destruction of rats would not be expected to have an early effect in reducing the number of infected larvae it might even in certain conditions increase the risk to human beings by depriving the larvae of their usual hosts.]

The vegetation of risky camp sites should be cut and removed the stubble should be sprayed with Diesel oil or kerosene and burned or it may be dealt with by a flame thrower

John W D Mcgaw

CLANCY C. F & WOLFE, D. M. A Rapid Staining Method for *Rickettsia orientalis* Science 1945 Nov 9 483

The following method of staining *Rickettsia orientalis* in smears from infected yolk sac membrane or other tissues gives good results and is quicker than that of SYVERTON and THOMAS [thus Bulletin 1945 v 42 879] The smears are dried in air and fixed by heat xylol is poured on drained off, and the slide is again dried in air It is then immersed for 5 minutes in a mixture of methylene blue and basic fuchsin—each 1 5 000 in distilled water—washed in tap water and dried. The dilute stain is best freshly prepared as required e.g. daily from stock 1 per cent solution of the two dyes.

J F Corson

O'Connor J L. Hirst's Haemagglutination Phenomenon exhibited by *Rickettsia orientalis* (Syn. *Tsutsugamushi*). *Med J Australia*. 1945 Dec 22, v 2, No. 25: 459-60.

Cultures of *Rickettsia orientalis* grown on the chorio-allantoic membrane of duck embryos caused agglutination of suspensions of red blood cells prepared from fowls, but positive results were obtained in only two of eight suspensions made from different fowls.

Hirst (Science 1941 July 4 22) (see also *Bulletin of Hygiene* 1942, v 17 686) described the agglutination of red cells of fowls by influenza virus, and CLARK and VAGLER (*Bulletin of Hygiene* 1944 v 19 164) found that the same phenomenon occurred with vaccinia virus, but only in about half of the red-cell suspensions that were tested.

In further experiments the author found that the serum of a patient convalescent from scrub typhus contained antibodies which inhibited the agglutination and that embryonic duck erythrocytes adsorbed most of the infecting agent from infected allantoic fluid. No agglutination occurred in any of six samples of red-cell suspensions made from one-day-old chicks. One sample each of human, sheep and guinea-pig cell suspensions also gave negative results. A description is given of the technical methods employed.

John W D Megaw

DE BURGH P. The Use of a Polysaccharide of *Bacillus proteus* OXK in the Diagnosis of Scrub Typhus. *Med J Australia* 1946 Jan. 19 v 1 No 3 81-3.

This study was undertaken to find whether *Proteus* OXK contained a polysaccharide-like substance corresponding to the one extracted by CASTAÑEDA and ZIA (1933) from *Pr* O\19 and found by them to be a minor antigen common to *Pr* O\19 and *Rickettsia prowazekii*. The author extracted a polysaccharide from cultures of *Pr* O\19 by trichloroacetic acid, after the method of BOVIER (1933) and with a solution of this he sensitized colloidal particles prepared according to the technique of LOEB (1922). Details of the methods are given. Sera of two patients convalescent from scrub typhus agglutinated the sensitized particles at the same titres (1-320 and 1-640) as were observed when *Pr* O\19 suspensions were used. The reaction is rapid, taking only 15 minutes. It appears to be more specific than the standard test because among eight samples of normal sera there were seven which gave positive reactions at a titre of 1-40 with *Pr* O\19 suspensions containing both the major and minor antigens whereas there were no positives with the sensitized particles, containing only the minor antigen.

The suspensions of sensitized particles had a life of about one week in the ice-box. It is suggested that in certain conditions the advantages of the reaction may outweigh the drawback involved in the laborious method of preparation, and that other antigens such as *Pr* O\19 may be used in the same way.

The polysaccharide was also used with success in a precipitin test but this was less satisfactory than the agglutination test.

John W D Megaw

TRAVASSOS J & VALLEJO-FREIRE A. Cracão antídoto de *Amelasma cayenne* para o preparo da vacina contra a febre maculosa. Artificial Breeding of *Amelasma cayenne* for the Preparation of Vaccine against São Paulo Spotted Fever. *Mem Inst Biol* 1944-1945 v 18 145-235 32 figs. (3 coloured pls) (38 refs.)

This interesting paper is really a monograph dealing with the preparation from ticks of a vaccine against the highly virulent São Paulo type of tick borne typhus. It consists of 90 large pages of text illustrated by 32 figures and three good coloured plates.

The disease is an important public health problem in the rural areas of the State of São Paulo where since the discovery of the disease in 1929 hundreds of deaths have occurred in widely distributed areas and in some places the disease interferes with the extension of agriculture.

Tick control was regarded as impracticable so that an organization was established at the Butantan Institute in São Paulo for the production of a vaccine by the method worked out by SPENCER and PARKER for the closely related disease Rocky Mountain spotted fever [see this *Bulletin* 1926 v. 23 361].

The pioneer worker on the vaccine in Brazil MONTEIRO and his assistant Edison DILLIS died of accidental infections acquired in the laboratory.

The chief vector *Amblyomma cajennense* is the most abundant tick in the State and is also the easiest to rear in the laboratory its life-history and identification are clearly described. Details are given of (1) the method of breeding the tick on a large scale (2) feeding the larvae on infected rabbits (3) maintaining the infected ticks till they reach maturity (4) the preparation and testing of the vaccine and (5) the protection of workers from accidental infection. All these procedures are fully described, with the help of numerous photographic and other illustrations which in themselves will be found very useful by those who undertake experimental work on ticks.

Little information is given about the output and distribution of the vaccine and the authors admit that evidence of its efficiency in the field is very difficult to obtain. It is regarded as likely that vaccination and six monthly revaccination give the same degree of protection as has been obtained by Spencer and Parker in Rocky Mountain spotted fever. The complete absence of laboratory accidents since the unfortunate fatalities mentioned above is regarded as significant in view of the great risk of laboratory infection despite the elaborate precautions that have been taken.

John W. D. Megaw

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## YELLOW FEVER.

ANTUNES W. & CASTRO A. Zona endêmica da febre amarela no Brasil. [Endemic Yellow Fever Area in Brazil.] *Boletim da Oficina Sanitária Panamericana* 1945 Nov. v. 24 No. 11 972-9. 3 maps & 2 graphs. English summary.

The endemic yellow fever area of Brazil based on experience of the last five years includes (a) all territory to the north of a line from the city of Brasília Acre Territory to Gurupá in Pará and thence along the Gurupá river to the Atlantic coast (b) the districts of Ilhéus and Itabuna at the east coast between the Contas and Pardo rivers. From the former area certain localities are excluded, viz Taracá Feijó Sena Madureira Amapari Brasília e Rio Branco in Acre Territory Porto Velho in Guaporé Territory Benjamin Constant Tabatinga, São Paulo de Olivença Fonte Boa Tefé Coari Codajaz Manaus Borba Itacaciara Manicoré Parintins and Humaitá in the State of Amazonas Obidos Santarém Monte Alegre Gurupá Currahinho and Belém in the State of Pará.

The demarcation plan of UNRRA [this *Bulletin* 1946 v. 43 124] does not distinguish between endemic and epidemic areas it includes a far larger area and would require periodical revision of the endemic areas to exclude quiescent epidemic areas.

J. F. Corson

"Field studies confirmed by laboratory experimentation, indicate that the mosquito *Harmogogus capricornis* is the chief vector of yellow fever in eastern Colombia. The object of the present article is to compare the seasonal variation in abundance of this mosquito with the seasonal distribution of human yellow fever in the region of Villavieja. The data for human yellow fever are based on the results of the examination of liver specimens obtained by the "Viscerotomy Service" over a period of 11 years. The data for mosquitoes are based on three years of standardized captures in a series of forest stations near Villavieja.

The climate of Villavieja is relatively uniform through the year except during the rainy season extending from December through March when rains are frequent. Human yellow fever fatalities reach a minimum in January and do not show a significant increase until November and December. In the dry season, June to September, there is no rain.

The climate of Villavieja is relatively uniform through the year except for a dry season extending from December through March when rains are comparatively infrequent. Human yellow fever fatalities reach a minimum at the end of the dry season (March) and do not show a significant increase until the second month of rains (June) reaching a peak in November and December. *Haemagogus* mosquitoes become relatively scarce during the dry season, but the population increases rapidly after the onset of the rains reaching a peak in June showing a slow but steady decline for the rest of the year except for a slight increase in November. It seems likely that the scarcity of yellow fever in the dry season is dependent on the low population level of *Haemagogus* mosquitoes and the post-dry season increase in yellow fever lags about a month behind the increase in mosquitoes. Human yellow fever remains at a high level through the rest of the rainy season, even though the mosquito population is declining and the peak of human yellow fever in November and December corresponds to only a slight rise in the mosquito population. It seems likely that the high incidence of yellow fever at this time is related to the habits of the local human population - it is customary to fill large areas of forest at this time with the object of burning the land in January and February leaving it ready for planting with the onset of the rains. The human population is thus in closer contact with the forest in November and December than at any other time of year.

LAKEBERT H. W. Jr. Studies on Susceptibility of Man to Yellow Fever Virus. *Amer J Trop Med* 1946 1: 33-46. [10 refs.]

The susceptibility of man to infection with yellow fever virus was investigated by Bognier *et al* (this Bulletin 1941 v 38 434) and BATES (ibid 1944 v 41 749) in the present paper additional experiments with various strains of yellow fever virus and several species of manimals are recorded. Altogether 335 manimals belonging to seven species were tested in which caught in various parts of Brazil, all except two of which were areas in which yellow fever was either epidemic at the time or had been reported previously. The animals were of various ages from newborn to adult, but most were young all were maintained satisfactorily under laboratory conditions. They were mostly inoculated subcutaneously but other routes were used in some cases for comparison. The seven strains of yellow fever virus were J.Z. (isolated in S. America in 1937) O.C. (S. America 1940) M.D. J.A. & Martinez (S. American jungle strains) Anbi (Africa) and the French neurotropic strain (Africa). The J.Z. and O.C. strains which had been isolated and maintained in *Macaca* monkeys were mostly used.

The viruses were titrated by intracerebral inoculation of mice and in the tests on marsupials small doses were inoculated as a rule. To test for circulating virus blood was taken from the heart on successive days and the serum inoculated intracerebrally into mice in the cases of *Didelphis* and *Metachirops* the serum was diluted as it is toxic for mice. After 30 days the surviving marsupials were bled to test for specific antibodies: no immune antibodies had been found before the inoculation of yellow fever virus.

The results of the tests are shown in seven tables from which and from the text the following details have been abstracted —

Species	Common name	No	Circulating virus present in	Immune bodies developed in*
<i>Didelphis marsupialis</i>	Common opossum	162	7	13/108
<i>D. paraguayensis</i>	White-eared common opossum	8	1	2/8
<i>Metachirops opossum</i>	Grey masked opossum	68	15	11/41 -
<i>M. nudicaudatus</i>	Brown-masked opossum	44	26	25/38
<i>Caluromys phillander</i>	Woolly opossum	12	11	8/9
<i>Marmosa cinerea</i>	Marine opossum	11	5	2/3
<i>M. incana</i>	Marine opossum	30	23	9/15

\*The proportion of survivors which developed specific antibodies.

The author concluded that *D. marsupialis*, *D. paraguayensis* and *M. opossum* were resistant to the strains used since only a few showed circulating virus and, in general the immunity response was poor. South American opossums are placental animals and the author thinks it unlikely that the newborn animals (in the pouch) acquired passive immunity from the milk of the mothers. The results in general were similar to those of Bugher *et al.* and Bates but the former authors considered these species to be susceptible. Bates regarded *M. opossum* as resistant. *M. nudicaudatus*, *C. phillander*, *M. cinerea* and *M. incana* were susceptible. It is interesting that *C. phillander* was susceptible to O.C. and Asiatic strains but not to J.Z. strain showing that certain animal species may be resistant to one strain and fully susceptible to another strain indistinguishable immunologically from the first. This suggests that there may be still other yellow fever strains to which certain species of marsupials are more susceptible.

J. F. Corson

## DENGUE AND ALLIED FEVERS

JOHNSON J. A. Jr. MARTIN W. B. & BRESLOW L. Dengue-like Fever on Okinawa. *Bull. U.S. Army Med. Dept.* 1946 Mar v 5 No 3 306-11 3 charts.

A short fever in regard to which the authors state that 'the diagnosis of dengue seems justified' made its appearance about the 7th April 1945 among the U.S.A. troops in Okinawa Island [26°N lat.]. The incidence increased gradually reaching its peak in the middle of July and then fell rapidly to zero about the middle of August. The rapid decline was associated with the establishment of mosquito control which is said to have become good by the middle of July.



## Tropical Diseases Bulletin

In April and May the most abundant mosquito was *Culex quinquefasciatus* [C. fatigans]. *Aedes albopictus* was rare and only occasional specimens of *Aedes aegypti* were found. In June and July *A. albopictus* could readily be found, but *C. quinquefasciatus* was still the most prevalent mosquito. No further mention is made of *A. aegypti*. The epidemiological evidence was therefore somewhat against the diagnosis of "true dengue" but *A. albopictus* despite its low density was thought to merit consideration as the possible vector.

The clinical aspects of the disease were regarded as differing from those of dengue in the relative infrequency of a secondary rise of temperature, the short average duration of the fever (3-4 days in a field hospital and 4-2 days in a clearing company) and the absence of a rash. In all other respects the disease conformed very closely to the generally accepted picture of dengue. In the field hospital, the percentage incidence of the chief symptoms and signs was as follows: Headache 83, chill or chilliness 82.5, orbital aches 100, backache 97.5, joint ache 100, adenopathy 85, conjunctivitis 95 and leucopenia 56.5. A definite reduction in the number of the polymorphonuclear leucocytes was observed by the 3rd or 4th day when there was a relative though not an absolute lymphocytosis.

The maximum incidence of the disease in one infantry division as shown in chart was at the rate of 275 per 1,000 per annum. Specimens of blood and serum have been submitted for virus studies so that presumably these charts are more suggestive of sandfly fever than of dengue.

John W. D. Megaw

HUENZ, W. Phlebotomen und Pappatacheber in Nordkaukasien. (Referat neber Arbeiten russischer Autoren u. eigene epidemiologische Beobachtungen.) [Sandflies and Sandfly Fever in North Caucasus.] *Dtsch. Tropenmed. Ztschr.* 1944 Apr-May v 48, nos. 7/10 182-92. [22 refs.]

This paper consists almost entirely of a review of recent work by Russian observers on sandfly fever in the region north of the Caucasus Mountains, between the Sea of Azov and the Caspian Sea, where the author had personal experience of the disease in the summer of 1942. He had already seen cases of fever clinically indistinguishable from sandfly fever in the Don-Donetz region, situated further north where sandflies are not known to occur so that the question arose whether the virus of sandfly fever was being transmitted by insects other than the sandfly or whether the disease was caused by a different agency.

It was not till 1927 that sandflies, including *Phlebotomus papatasi* were found to occur in Northern Caucasus, indeed so recently as 1934 an outbreak whose clinical features were those of sandfly fever was regarded as one of "mosquito disease". In 1935 widespread outbreaks occurred in the region and were attributed to virus transmitted by *P. papatasi*.

The disease was closely studied, especially by Mosinkowsky and his colleagues who in 1936-37 published a series of articles on the subject [see this Bulletin 1937 v 34 858]. There seems to have been no important difference between the clinical features of the disease and those of sandfly fever in other countries.

In the summary of the experimental work by Russian observers, reference is made to successful immunization of human beings by injecting the virus after previous injections of convalescent serum and to the passage of the virus through the eggs of experimentally infected sandflies to their offspring and through the yolks of hens' eggs up to 48 passages.

References are given to 20 articles on the subject by Russian workers during the years 1936-1940

*John W D Meigs*

NAJERA ANOULO L. La fiebre de pappataci en España. [Sandfly Fever in Spain.] Reprinted from *Semana Med Española* 1946 Jan. 26 v. 9 No 359 87-98 5 figs. [Bibliography]

## PLAGUE.

DEVIGNAT R. Aspects de l'épidémiologie de la peste [Standardization of Epidemiological Surveys in Plague.] *Bol Oficina Sanitaria Panamericana* 1945 Oct v. 24 No 10 895-906 1 chart & 1 fig English summary

In an introduction Dr Devignat refers to the classical opinion originated by the Indian Plague Commission that the rôle of vector in plague epidemic and epizootic attaches to the flea *Xenopsylla cheopis* and that subsidence of an epidemic is correlated with variation in the flea index. He cites exceptions and objections to this view and brings forward a scheme of standardization for the epidemiological study of plague which would apply to local conditions and yet be comparable with conditions prevailing elsewhere. He has applied his scheme to the study of plague 1941-1943 in the region of Lake Albert in Belgian Congo. The scheme now proposed permits the inclusion of the *Rattus coucha ugandae* of Blukwa with its infestation by *Xenopsylla* fleas among the domestic rodents.

There are according to Devignat three fundamental plans of plague activity, the sylvatic and domestic murine plans and the human plan with six methods of possible contagion. These are intersylvatic, interdomestic, interhuman, sylvo-domestic, sylvo-human and domestico-human. He has devised a linear equation to determine Q the common index of epidemiogenic or epizootic transmissibility based on modes of transmission. Various constants enter into the equation such as K the constant of receptivity,  $k$ ,  $k'$ ,  $k''$  constants of vector and variables in the shape of indices  $i$ ,  $i'$ ,  $i''$  rat flea indices and  $t$ ,  $t'$ ,  $t''$  flea burrow indices. The technique for development of this standard scheme is given in detail. A chart is figured to show the application of the plan to Lake Albert. It may be noted that pulmonary plague is excluded from this suggestion of a standard plan to summarize all the epidemiological aspects of plague in various countries. *W F Harvey*

MACCHIAVELLO A. Instrucciones para el diagnóstico tratamiento y aislamiento de enfermos de peste bubónica, y para la recolección de muestras destinadas a exámenes de laboratorio [Instructions for Diagnosis, Treatment and Isolation of Plague Cases and for Laboratory Specimens.] *Bol Oficina Sanitaria Panamericana* 1945 Aug v. 24 No 8 704-12.

These instructions are set out in a series of 23 detailed and clear paragraphs. They should leave no practitioner who is confronted with the possibility of plague in any doubt what he should do. The first paragraph reads—The present ordinance establishes the rules for diagnosis isolation and laboratory examination including human autopsy of bubonic plague as well as the simple examination required in every notification of certain or suspected human or rodent plague. The several instructions follow and the article ends with the printed form for cases of plague.

*W F Harvey*

WATSON N. E. & McMAHON Margaret C. Plague Treatment of Experimental Animals with Streptomycin, Sulfadiazine, and Sulfapyrazine. J. Lab. & Clin. Med. 1946 Mar., v 31 No 3 323-32, 1 fig.

Sulphonamide therapy has been extensively tested in plague, and the value of sulphadiazine has been established. The authors have now tested streptomycin a product of Actinomycetes griseus and appropriately controlled by comparison with sulphadiazine. Mice and guinea pigs were the animals used and infection was induced by inoculation and, also in guinea pigs more naturally through fleas. Streptomycin was given subcutaneously dissolved in normal salt solution. Sulphonamides were suspended orally by syringe or in capsules. This therapy was given after infection, and indicated that streptomycin had definite value. Summarizing the authors say — (1) Three hundred and thirty four white mice were inoculated with plague and one-half were treated in groups with different amounts and varying dosage of either streptomycin, sulfadiazine or sulfapyrazine. The other one-half were used as controls. Under the treatment schedules finally adopted, while all the corresponding controls among each lot of from eighteen to twenty, died of plague. (2) Forty-eight guinea pigs were likewise inoculated and one-half were treated with streptomycin in two groups after clinical evidence of infection had developed. All survived but eight had residual buboes at necropsy. Twenty-three controls died with plague. (3) One hundred and six guinea pigs were infected through flea transmission. After the disease was evident clinically fifteen were treated with streptomycin and fourteen survived. Sixteen received sulfadiazine and fourteen survived. Three survived among all the survivors had residual buboes at necropsy. (4) Clinical recurrences appeared frequently under the treatment schedules used with streptomycin and sulfapyrazine but not with sulfadiazine.

KLINGENSMITH, C. W. A Note on the Natural Occurrences of Fluoroacetic Acid, the Acid of the New Rodenticide "1080". Science 1945 Dec. 14 622-3

The sodium salt of monofluoroacetic acid has recently been advocated as a rat poison [this Bulletin 1946 v 43 331]. The acid itself has been shown by MAHAI (Onderstepoort J. 1 of Sci. 1943 v 18, 203-6 1944 v 20 67-73) to be the toxic principle of *Dichapetalum* (= *Chamaecha*) cynosuroides called Gifblaar. Another species in the genus *D. toxicaria* is a notorious poison in South Africa. Another species in the genus *D. toxicaria* is a notorious poison in Sierra Leone where it has been used by colonists for destroying rats. R. B. Freeman.

MONSANTO CHEMICAL COMPANY "1080" Rodenticide to be sold only to Pest Control Operators. Pests. 1946 Jan. v 14 No. 1 23.

Owing to its very high toxicity "1080" will not be on sale at any time to the general public. The lethal dose for man is believed to be one-fiftieth of an ounce — about 8 mgm. per kgm. for a man of 60 kgm. (10 stone). No antidote is known. It is recommended for use at 0.04 per cent. on oats, one-fiftieth of an ounce to three pounds. Cases of deaths of dogs and pigs, presumed to be caused by eating poisoned rats, are recorded. Though not stated here, "1080" is sodium fluoroacetate. [A verbally identical note except for statement about danger to domestic animals, occurs in *Chemurgic Digest* 1946 Jan. v 5 22. There was an even briefer summary of the same press release in *Chem. Engng News* 1945 v 23 2367.] R. B. Freeman.

UPTON R. G. The Use of Antu as a Rodenticide. *Pests* 1945 Dec. v 13 No 12 22.

Extensive field tests have been carried out with a-naphthylthiourea in Texas. It was mixed at 50 per cent. with 5 per cent DDT and 45 per cent. inert powder and dusted in burrows and runways which method gave very poor results. The majority of the rats were *Rattus rattus alexandrinus* which species is known to be much more resistant to this poison than *R. norvegicus*. It is very slow in action deaths being recorded up to eight days. A considerable number of cats were killed. Chickens are said to be very resistant a tenth of an ounce being required to kill a two-pound bird (nearly 3 grams per kilo)

R. B. Freeman

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### CHOLERA.

YACOB M. & CHAUDHRI J. R. A Note on the Spread of Cholera Infection through Aerated Drinks. *Indian Med Gaz* 1945 Dec. v 80 No 12 634-6

With the outbreak of epidemic cholera public health authorities tend to recommend or impose standard regulations as to food and drink upon the populace. Many of these regulations have been handed down for generations and have not been subjected to actual test. This certainly applies to aerated drinks and perhaps to ice. The authors have tested soda water and lemonade for their capacity to promote the growth of cultures of *V. cholerae* or as the case may be their vibriocidal action. These waters have a pH of 6.8 as compared with control water of 7.8 and the gas which was not allowed to escape had a pressure varying from 125 to 150 lb. For the ice experiments water infected with cholera culture was converted to ice and was used after 24 hours to cool the aerated drinks. The conclusions are very interesting — The experiments described show conclusively that given sufficient time an aerated drink even if infected with cholera is rendered harmless by its own action. It is not certain whether the vibriocidal action is due to lowered pH or to pressure of the gas although under the same experimental conditions only one bottle out of five containing non-aerated lemonade gave a growth of cholera vibrios. It also seems likely that cholera infected water when converted into ice and served in drinks may also not prove harmful. W. F. Harvey

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### BACILLARY DYSENTERY

CHEEVER F. S. Dysentery Outbreak aboard Naval Vessels in San Pedro Bay, Philippine Islands. *U.S. Nav Med Bull* 1946 Apr., v 46 No 4 479-84

During the months of July and August 1945 an outbreak of bacillary dysentery occurred on ships of the Third Fleet and Service Squadron 10 anchored in San Pedro Bay Philippine Islands. More than 6,000 cases were reported during this period. The etiologic agent was *Shigella flexneri* III (VIII). The disease was clinically mild and only 3 deaths were recorded.

The original focus of infection was apparently the native population. Naval personnel appeared to have become infected through contact with native food and drink either ashore on the recreation beaches or afloat by patronizing bumboats. The subsequent inter ship spread was probably caused by polluted

harbor water (small-boat personnel being particularly hard hit) and by personal contact between the crews of two or more ships that were tied up together. Once the disease became established aboard a crowded ship, it proved extremely infectious and hard to control in spite of the usual sanitary measures. Infected food handlers, convalescent carriers and subclinical cases probably contributed to the spread of the disease. Flies may have been involved in the genesis of the epidemic on the beach, but they played no role in the subsequent spread of the disease in the anchorage. No evidence was disclosed that fresh water obtained by distillation of harbor water was contaminated, and the epidemiologic picture was not one of massive water-borne infection.

Experimentally it was proved that strains of the specific organism recovered comparatively late in the epidemic could survive at least 2 days in sea water and that they were relatively resistant to the bacteriostatic action of sulfa diamine and sulfathiazole. This property of drug fastness is one explanation for the noteworthy failure of chemoprophylaxis to check the epidemic."

MOORE, F. J., HESSEL, J. F., SIMONSEN, D. G. & MARMORSTON, JAMES with the technical assistance of H. LEWELLYN, F. KAPLAN, F. GOLDEN, N. ANDERSON & E. JAFFE. Experimental Basis of Sulfonamide Therapy in Bacillary Dysentery. *J. Infect. Dis.* 1946 Jan.-Feb., v 78, No 1 25-31 [26 refs.]

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

BROWN, A. G. Experiences with Amoebiasis in an Evacuation Hospital. *War Medicine* Chicago 1945 Nov.-Dec., v 8 No. 5 319-24

In a 400-bed American Evacuation Hospital, during two years' service in North Africa and in Europe, intestinal amoebiasis was diagnosed in 243 patients and hospital personnel. The majority of these had been hospitalized for gastrointestinal symptoms. A survey of the hospital personnel, after 18 members had been treated for acute amoebic dysentery, showed that 65 of 298 (21.8 per cent.) were infected with *Endamoeba histolytica*. Diagnosis was at first made in the usual manner by the examination of fresh specimens of stool. Subsequently Schaudinn-fixed smears were stained with iron-alum-haematoxylin, as difficulty was experienced in identifying cysts and "pre-cysts" in fresh preparations. A rapid method of fixation and staining, taking little more than one hour is described.

Treatment, where undertaken, was daily for 10 days with emetine injections, accompanied, and followed after a week's interval, by courses of carbarsone or chinolone, as recommended by U. S. Army Headquarters, North Africa. One week after completion of the second course, three stools were checked. In only 1 case were *Endamoeba histolytica* cysts still present after the two courses, and this patient was evacuated for further therapy. In a few cases amebae other than *Endamoeba histolytica* were not all destroyed by the course of therapy."

[The difficulty experienced generally by service pathologists in differentiating the morphologically characteristic cysts of the intestinal protozoa in fresh unstained preparations of faeces is perhaps not unduly hard to understand. But the ease with which these pathologists can specifically identify, in fresh preparations and after a saline purge, the much less obviously characteristic vegetative stages of these same parasites is more difficult to grasp. The apt "it moves—it's an amoeba. It has engorged red cells—it's *histolytica*," reasonably accurate for the detection of the acute amoebic dysentery, not be regarded as adequate for the purpose of a survey of

infection rates. This does appear to have been recognized to some extent in the study recorded in the present paper as staining methods after fixation were adopted.]

A R D Adams

LUCAS R. B. Culture Methods in the Diagnosis of Amoebiasis. *J Roy Army Med Corps* 1945 Nov v 85 No 5 249-51

Using Loeffler's serum slopes covered with Ringer's solution to which egg albumin and rice starch were added the author attempted to cultivate *E histolytica* from the faeces of 405 patients sent to the laboratory of a military hospital in an area in which amoebiasis was endemic. *E histolytica* was discovered in 18 by direct microscopical examination and all these gave a positive culture. In addition positive cultures were obtained in 24 cases in which amoebae were not discovered by the microscope. It is concluded that culture of faeces for *E histolytica* as a routine measure can be of considerable value in the diagnosis of amoebiasis.

C M Wenyon

LAWLESS D K. Detecting Intestinal Protozoa. Saline-Iron-Haematoxylin Solution for Wet Smears. *Amer J Trop Med* 1946 Jan v 26 No 1 133-4

Cysts and trophozoites of intestinal protozoa in faeces are easily distinguished from similar objects and from the background if fresh slide preparations are made with the following mixture: normal salt solution 75 cc. 0.5 per cent. haematoxylin solution 10-15 cc. 4 per cent. ferric ammonium sulphate 0.25 cc. A small particle of faeces is emulsified in a drop of the solution to make a thin film under a coverslip; the protozoa are seen against a black-stained background.

J F Corson

HANZAH N A. Amoebic Appendicitis. *J Palestine Arab Med Ass* 1946 Mar v 1 No 3 72-4

Of 50 appendices removed consecutively at the Government Hospital Haifa Palestine 13 had amoebic ulcers (amoebae present) 9 had other ulcers 21 had diffuse infiltration and 7 had worms 4 were gangrenous but none of these was amoebic.

In 12 of the 13 cases with amoebic ulcers the appendix appeared normal or slightly thickened externally and the mucosa looked normal except for two or three greyish sanguineous sloughs covering ulcers with undermined edges; the ulcers were mostly limited to the mucosa but in a few cases they extended to the serous coat.

These 13 cases were diagnosed before operation as subacute appendicitis; they had a history of slight pain in the right lower abdominal quadrant for months or even years and tenderness over McBurney's point was present in all.

The author concludes that from 20 to 30 per cent. of cases of subacute or chronic appendicitis in Palestine are of amoebic origin. If amoebae are found in the stools before operation medical treatment should first be given and operation should be done later to prevent relapse.

J F Corson

GOLDEN R. & DUCHARME P. The Clinical Significance of Deformity of the Cecum in Amoebiasis. *Radiology* 1945 Dec. v 45 No 6 565-80 6 figs [14 refs]

Amoebiasis is common in the United States and its diagnosis may be difficult. Sixty-seven patients (in 58 of whom *E histolytica* was recognized in the stools and in 9 of whom this organism was assumed to be present though not actually found) were radiographed after a barium meal (27) or after a barium enema (18)

or after both (22). Thirty three of the 67 patients suffered from diarrhoea, 9 complained of various abdominal symptoms but not of diarrhoea and the remaining 25 were either free from abdominal symptoms (18) or there was inadequate information in respect of these (7). In 30 of the 67 including 18 of those complaining of diarrhoea, and 21 of the microscopically proven cases of amoebiasis deformity of the caecum was observed radiographically. This deformity varied considerably in some cases it was slight and consisted of narrowing of the tip in others the caecum was markedly shrunken, but its outline was generally smooth and only rarely irregular. Where deformity occurred there was usually localized tenderness over the caecal area and in some cases pressure apparently accentuated the deformity. In no case was narrowing or intrinsic deformity of the terminal ileum seen, although in one instance obliteration of the folds and the smoothness of the shadow suggested oedema of the ileal mucosa. This cleared after specific anti-amoebic treatment.

Five patients with caecal deformity were re-examined after treatment. In four there was "relaxation of the caecum" suggesting improvement. In the fifth case with a markedly shrunken caecum there was no change. From this the authors deduce that the caecal changes produced by amoebiasis in its later stages are irreversible. They conclude that caecal deformity demonstrable on radiography is likely to be seen in over one-third of cases of amoebiasis more particularly in those with intestinal symptoms. It may give a valuable pointer to the diagnosis but its absence does not exclude a diagnosis of amoebiasis.

A R D Adams

Isaac F Roentgen Findings in Amebic Disease of the Liver *Radiology*  
1945 Dec., v 45 No. 6, 581-7 5 figs.

Amoebic involvement of the liver is the most common complication of amoebic dysentery. It is more common in visitors to the tropics than in the natives. Of 222 cases of amoebic dysentery in an Army Hospital overseas 32 (14 per cent.) suffered embolic liver infection. Two stages of liver trouble were seen a diffuse hepatitis (without jaundice) and, later amoebic abscess or multiple abscesses. Clinical differentiation of the stages is difficult unless aspiration or drainage is done. These are rarely necessary if early specific treatment is instituted, and so most of the author's cases were designated amoebic hepatitis. On X-ray examination about half his patients showed no signs or at most downward enlargement of the liver. These were probably cases of diffuse amoebic hepatitis. The other half showed doming of the right diaphragm with flattening of the costophrenic sinus. The doming may be restricted to the outer portion of the diaphragm or it may be in the mesial portion and the cardiophrenic angle is then obliterated. Sometimes the elevation is limited to the middle portion of the right diaphragm and the costophrenic and cardiophrenic angles are sharpened. Elevation of the right diaphragm is the most unequivocal sign of amoebic liver abscess. On screening limitation of movement with sluggishness or fixation of the right diaphragm may be seen. The right lower lung field may show changes resembling an atypical primary pneumonia owing to compression of the base by the raised diaphragm or to an interstitial pneumonitis or to partial atelectasis. There may be a pleural reaction with thickening of the pleura and effusion into the costophrenic sulcus. This probably arises from rupture of the liver abscess into the right pleura and the chest signs may then mask the causative liver lesion.

Most cases of amoebic liver disease respond to medication without operative interference or aspiration. Illustrative cases are cited, with reproductions of radiographs.

[No mention is made of the possibility of variation in the site of amoebic abscesses in the liver. It is apparently assumed that these *always* occur in the upper portion of the right lobe.] *A R D Adams*

COTTRELL J D & HAYWARD G W. The Effects of Emetine on the Heart. *Brit Heart J* 1945 Oct. v 7 No. 4 168-70 2 figs

Changes in the electrocardiogram blood pressure and pulse rate produced by emetine and emetine bismuth iodide have been studied in soldiers under treatment for amoebiasis. All were otherwise healthy and the initial cardiograms were normal. Diminution or inversion of the T waves occurred in one or more leads in 25 out of 32 cases receiving emetine and in 12 cases there was an increase in the P R interval of from 0.02 to 0.04 sec. Similar changes occurred during treatment with emetine bismuth iodide 7 out of 8 cases showing diminution in T waves and prolongation of the P R interval. The cardiogram returned to normal 8-12 days after the completion of treatment. The effect on the blood pressure and pulse rate of both drugs was insignificant and in no case was there any clinical evidence of myocardial insufficiency.

BERBERIAN D A. Treatment of Lambliasis with Acranil. *Amer J Trop Med* 1945 Sept v 25 No 5 441-4 [27 refs.]

The author has treated 50 cases of giardia infection in children with Acranil [see this *Bulletin* 1945 v 42 909]. The dose of the drug varied around 0.1 gm. twice or thrice daily for five days. In some cases an initial dose of 0.2 gm. to 0.5 gm. commenced the course. Following the treatment five weekly examinations for giardia infection were carried out. It appeared that in all the 50 children as well as in three adults Acranil had eradicated the infection. It is noteworthy that other protozoal and helminthic infections were unaffected by the drug which was well tolerated by all the children though a slight coloration of the skin occurred. *C M Wenyon.*

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES.

ADVIER. La fièvre récurrente et ses accidents nerveux. [Relapsing Fever and its Nervous Manifestations.] *Les Grandes Endémies Tropicales* (Onzième Année) 1939 Paris pp 33-48.

A useful summary of the history of relapsing fever with special reference to the occurrence of the disease in the French Colonies. The title of the article however is somewhat misleading since little more than two pages are concerned with relapsing fever as it affects the nervous system. *E Hundle*

MOLLARET P & DIGO R. Association probable d'une pasteurellose et d'un biokoshio (sodoku par morsure de chat) [Probable Association of a *Pasteurella* Infection with Cat-Bite Fever] *Bull et Mém Soc Méd Hôpît de Paris* 1946 No. 3 4 5 6 & 7 137-40 1 fig [18 refs.]

## LEPROSY

NEWMAN P P. A Visit to an Indian Leper Colony. *Brit Med J* 1946 Apr 20 616.

PRABHU M N. Leprosy of the Upper Respiratory Passages. *Leprosy in India* 1946 Jan v 18 No 1 10-12.

The author who was resident medical officer in charge of ear nose and throat hospital cases at a Madras hospital reports the results of examinations



carried out at the Silver Jubilee Leprosy Clinic including bacteriological examinations during a period of six months. The evidence indicates that nasal infections are the result of general rather than of local infections. In simple macular neural leprosy the nose is seldom if ever infected but in major tuberculoid leprosy nasal lesions are not uncommon. The nasal mucous membrane first becomes congested and oedematous with greyish, whitish or yellow inflammatory spots, and it bleeds easily. *Lepra* bacilli can be found in small number only and blocking of the nose results with the formation of crusts. Later ulceration occurs, the septum may be perforated and destruction of cartilages with deformities may result. The mouth tongue and pharynx may become involved in advanced lepromatous disease and perforations of the hard or soft palate may resemble those due to syphilis. Nodules occur and also leprosy glossitis which may be extremely painful. In such cases the larynx may become similarly affected, first with thickening of the epiglottis with spread to the vocal cords either as an ulcerative or a fibrotic condition. Much swelling and oedema may necessitate tracheotomy.

L. Rogers

Mix E. Elephantiasis and Septic Infection. *J Trop Med & Hyg* 1945  
Dec-1946 Jan v 48 No 6 145-8, 3 figs.

In this paper a comparison is made between lepromatous leprosy and filarial elephantiasis as regards secondary septic infection and the development of pachydermatous conditions in both cases associated with lymphatic obstruction and with periodic inflammatory changes. In the filarial disease the febrile attacks are associated with monthly parturition of the adult female worms, with the production of very large numbers of embryos as shown by ROGERS, and are accompanied by lymphangitis which may be of septic origin. Allergy is also thought to play a part in this process. In lepromatous leprosy the frequent febrile reactions may similarly be caused by secondary septic organisms by blocking of small lymphatic vessels and by allergic reactions like those produced by the injections of protein matter derived from *lepra* bacilli, such as followed by the use of Dharmendra's lepromin, or by the administration of iodides, as shown by Venn himself. An illustration is given which shows great swelling of the face during an acute lepra reaction and another shows a pachydermatous condition of the face. Attempts to control lepra reactions by sulphonamide drugs failed, but more recently promin and diason, which inhibit the growth of the tubercle bacillus have proved more effective, especially in inflamed eyes and ulcerated noses. Sulfaseptazine given intramuscularly cleanses septic leprotic ulcers rapidly. The action of penicillin resembles that of diason and promin in advanced lepromatous cases and as penicillin is inert against tubercle bacilli and probably against *Mycobacterium leprae* the action of all three is probably on the septic infection. All this points to septic infections playing an important part in the causation of lepra reactions.

L. Rogers

D & SERRA D T. Lepromin Skin Tests in Boeck's Sarcoid. *Amer J Hyg* 1946, Nov., v 53 No. 6 519-21 1 fig

tests in ten cases of Boeck's sarcoid, including

11. The clinical symptoms were typical examinations. In seven the lepromin also negative to tuberculin. In the reactions and in two of them tuberculin of active tuberculosis gave positive that Boeck's sarcoid is an attenuated

L. Rogers.

HARRELL, G T & HORNE S F The Reaction to Lepromin of Patients with Sarcoid or Tuberculosis compared with that of Patients in General Hospitals with a Discussion of the Mechanism of the Reaction *Amer J Trop Med* 1945 Nov. v 25 No 6 523-35 7 figs. [17 refs.]

This paper also deals with lepromin tests to determine if Boeck's sarcoid may be caused by the *Mycobacterium leprae* as suggested by the clinical and pathological resemblances between certain cases of sarcoid and tuberculoid leprosy. It deals with 70 patients tested with lepromin: they included 5 with sarcoid, 5 with active tuberculosis, 41 with healed or inactive tuberculosis who were suffering from a variety of chronic diseases, and 18 with a variety of acute and chronic diseases. The authors regard early erythematous reaction with lepromin as less specific than the later infiltration and ulceration which occurs at the site of the lepromin injection in positive cases. Full details of the tests are given and the results tabulated. From a study of these the authors come to the following conclusions. In patients with sarcoid the reactions are slight and infrequent: they give no indication that sarcoid is atypical tuberculoid leprosy. In a control group in the U.S.A. the incidence of intense or moderately intense lepromin reactions is less than in endemic areas of leprosy in the tropics. The high incidence of strong late lepromin reactions in active tuberculosis suggests the presence of common sensitizing antigens, possibly soluble protein or polysaccharide. It is also suggested that a lipid may be the active chemical fraction. If tuberculosis can be ruled out, lepromin may prove useful in the diagnosis as well as the prognosis of leprosy. The authors suggest that leprosy like tuberculosis may be a disease of high contagion, slow progression and high curability, requiring repeated regular exposures to the infecting organism. Attempts should therefore be made by frequent inoculations of living organisms into animals over a long period, with a view to their infection. As the living monocyte appears to furnish a substance essential for the growth of the *Mycobacterium leprae*, attempts should be made to cultivate it by the inoculation of tissue cultures of monocytes or of chick egg chorio-allantoic membrane with infected material.

L. Rogers

#### CORRECTION

Professor DE SOUZA ARAUJO has called attention to the fact that for the experiments referred to in the abstract in this *Bulletin* 1945 v 42 1010 he used his original cultures of acid fast bacilli isolated from leprosy material and not emulsions of material rich in Hansen's bacilli as stated in the abstract — Ed

SLOAN T B M The Role of Propaganda in the Control of Leprosy *Leprosy in India* 1946 Jan. v 18 No 1 15-22.

The subject is dealt with on very general lines with special emphasis on education of the public. The author thinks that too much attention is being paid in India to treatment rather than to isolation of infective cases. Legislation is not needed for the control of patients with neural leprosy, but more persuasion is required for the isolation of lepromatous cases. Propaganda should be prepared by a professional publicist and radio talks and discussions should be arranged. Posters and slogans should be displayed in schools and public buildings so as to combat common prejudices among the illiterate. The author supports the view that the word 'leper' should not be used. School teachers should be instructed on the subject as well as employers of labour who should know that 75 per cent. of all cases are uninfected. L. Rogers

BLOSS J F E. The Control of Leprosy among the Azande, Anglo-Egyptian Sudan. *Trans. Roy Soc. Trop Med & Hyg* 1946 Apr v 39 No 5 423-36 1 map.

This valuable report brings up-to-date information on work for the control of leprosy in the heavily infected humid southern Sudan where much leprosy was discovered during operations against an outbreak of sleeping sickness. Dr ATKEY the P.M.O. originally ordered a leprosy survey which was carried out by Dr CRICKSHANK in 1929 with the discovery of 8 400 cases within two years, representing 3.3 per cent. of the population whose diet was deficient in animal proteins. In 1929-30 a total of 5,500 lepers—some 80 per cent. of the known cases in the district—were transferred with their families to two large settlements, at Sougas Yubu and Li Rangu, and treated mainly by Alepol intravenously which was found to be the most effective preparation. By the end of 1931 30 per cent. of the patients had improved, and 40 per cent. more were discharged as quiescent and uninfected. Advanced lepromatous cases were now segregated in special camps to diminish the chances of infection. In 1935 WOODMAN (*Sudan Vet. Serv Ann Rep* 1935) estimated the disease incidence at 7 per cent. of the population and reported that the records of 3,500 cases [see this *Bulletin* 1938 v 35 295] showed good results from treatment with chaulmoogra derivatives for periods not exceeding 3 or 4 years after which no further benefit accrued. He considered that the Li Rangu settlement, with 25 sq. miles of land then the largest in Africa, was of value in isolating the most infective cases and in facilitating treatment. In 1935 the Li Rangu settlement figures were —

Advanced cases segregated	204
Under observation or treatment in settlement	1 021
Discharged cases, cures and quiescent, living in settlement	951
Discharged cases living outside settlement	513
Total	2 689
[Total cured or quiescent (951+513) 1 464 (54.4%)]	
Outside cases which had never been in the Settlement	809
Total	3 498

This settlement however was overcrowded.

In 1939-40 a new survey and census was made and yearly inspection of the whole population was being carried out in 1941 a card index overcame difficulties in registration of patients. The total known cases had fallen to 1,855 and the new cases had declined from 253 in 1939 to 186 in 1941 and 86 in 1942.

Conditions in the settlement have now been improved, and agricultural work is paid for this furnished almost all the food crops for much increased rations. During the war Alepol supplies ran out and treatment has been disappointing. The age incidence now shows that less than 12 per cent. of the known cases are in persons under 20 years of age, against 21 per cent. in 1930. "This points to (a) the disease being under control, and (b) that a decrease rather than an increase in the number of cases is to be expected in the future." A gradual decentralization is now being aimed at by organizing a number of local, small, chief's colonies in place of one very large settlement, coupled with an increase in public health activities and improvement in the standards of living.

L. Rogers.

CHANDY P J. The Problem of the Discharged Patient. *Leprosy in India* 1946 Jan., v 18 No. 1 13-14.

This is a short note by the medical officer of the Fyzabad Leper Home and Hospital, which deals with 40 cases discharged during the previous six years.

Patients with arrested disease are often unwilling to leave the institution to make room for more suitable patients on account of social prejudices and difficulty in obtaining employment under favourable living conditions. Eight of the 40 discharged cases had relapsed not a very high rate but enough to make an employer loath to run any risk. Discharged patients may meet with difficulties in returning to live in their own villages patients who show any deformity are especially viewed with suspicion. Two developed tuberculosis which is common among leprosy patients. A few can be employed after recovery in leprosy institutions. The author suggests that industrial and agricultural settlements should be started near each leprosy institution which will ultimately become self-supporting and provide the best solution of the problem.

L. Rogers

PRUDHOMME R. O. Conservation de la vitalité du bacille de Stéfansky dans des lépromes desséchés [Conservation of the Vitality of Stéfansky's Bacilli.] *Bull Soc Path Exot* 1944 v 37 Nos 11/12 338-44

MARCHOUX and SOREL (*Ann Inst Pasteur* 1912 p 1) have shown that when Stéfansky's bacilli of rat leprosy are dried for two days over sulphuric acid in a vacuum they are no longer infective to rats and that they also die when preserved for 15 days at 37°C in physiological saline. The vitality of the organisms can be tested without animal inoculation if to 1 cc. of a pure emulsion of the bacillus is added 1/20 cc. of a solution of orthocresol-endo-2-6 dichlorophenol N/10 000 in boiled distilled water and the blue mixture is placed in an ampoule which is sealed after removal of the contained air. If the bacilli are living at the end of 24 hours the contents of the ampoule will have become decolourized but not if they are dead. By the use of this test and by the inoculation of rats the authors have found that bacilli contained in a leproma frozen and crushed at -28°C. and then dried and kept in a vacuum at from 0° to 4°C. retained their virulence for rats for over one year but if kept in the presence of air they died. Lepromata dried over sulphuric acid also kept their virulence for over a year in a vacuum, but not in air.

L. Rogers

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## HELMINTHIASIS

TARR L. Effect of the Antimony Compounds, Fuadin and Tartar Emetic, on the Electrocardiogram. A Preliminary Report. *Bull U.S. Army Med Dept.* 1946 Mar v 5 No. 3 336-9 1 fig

Electrocardiograms were taken in 150 patients who had returned from abroad where they had suffered from schistosomiasis and had been treated with Fuadin or tartar emetic or both at times varying from 22 to 112 days previously. They showed no clinical symptoms or signs of organic heart disease and all except four of the electrocardiographic tracings were normal. In 66 patients ova of *Schistosoma japonicum* were present in the faeces and the patients were given further treatment with antimony. Electrocardiograms were taken under standard conditions before during and after this treatment.

Fuadin—Intramuscular injections every other day of a 6 per cent solution to a total of 65 cc. (0.566 gm. of antimony) in 14 injections—was given to 28 patients, while tartar emetic—intravenous injections every other day of 0.5 per cent. solution to a total of 320 cc. (0.576 gm. of antimony) in 15 injections—was given to the other 38 patients.

The only change in the electrocardiogram was a decrease in the voltage of the T wave of different degrees which the author classifies as one plus two plus,

three plus and four plus, respectively only the last two being significantly different from normal tracings these however might easily have been interpreted as indicating myocardial damage or even coronary occlusion. The three plus or four plus changes occurred in 12 (31 per cent.) of the 38 patients treated with tartar emetic and in only two of the 28 who were treated with Fuadin. There was no apparent relationship between the maximum changes in the electrocardiogram and toxic effects of the drugs and in no case was the course of treatment altered because of such changes. The return to a normal cardiogram began some days after the end of treatment and was usually complete within a month.

The author regards the electrocardiographic change as a transient reversible effect of trivalent antimony on the heart and its only importance is the possibility of mistaking it for serious myocardial damage. [The author somewhat misrepresents the findings of MAIZER and KRAUSE (this Bulletin 1940 v 37 487) in 7 of their 12 cases the electrocardiogram showed either a definitely pathological tracing during the antimony treatment (3 cases) or a curve which "suggests the suspicion of an altered function of the cardiac muscle" (4 cases)]

J. F. Corson

TORRES C. M. & PINTO C. Mecanismo de eliminacão dos ovos de *Schistosoma mansoni* estudado no tath (*Euphractus sexcinctus*) [Mechanism of Elimination of the Eggs of *S. mansoni* in the Armadillo.] 4<sup>ta</sup> Acad. Brasileira de Ciências 1945 Dec. 31 v 17 No 4 271-2 2 figs. on pls.

The armadillo to which the authors refer died 94 days after infection, and at autopsy 86 female and 23 male *S. mansoni* were found in the liver and two of each sex in the pancreas. In the walls of both small and large intestine there were numerous granulomata and eggs, but there were interesting differences in the distribution of the lesions between the small and the large intestine. In the small intestine, granulomata and eggs were always localized in the submucosa, never above the muscularis mucosae the small intestine is evidently not the route by which eggs are passed to the exterior. In the large intestine on the other hand, the granulomata and eggs are most numerous in the mucosa itself, and are rarely seen in the submucosa. Elimination of eggs into the faeces is therefore exclusively performed in the large intestine.

The mechanism of elimination is complex. It depends on various factors — (1) the structure of the intestinal wall and its vessels (2) the extrusion of the eggs from the capillaries and their fixation in the mucous coat at the level of the fundi of the crypts of Laeberkuhn (3) the formation of cellular infiltration round the eggs (4) histolysis of the walls of the crypts by products elaborated by the eggs (5) elimination to the exterior along with the intestinal secretions. The important part of this process is the elaboration of histolytic substances by the embryo. In the large intestine the authors found cystic dilatation and hypertrophy of the glands which may have been the precursors of adenomatous polypi.

Charles Walcocks.

HILLEMANN P., VARAY A., DERRAY J. R. & DOUGUET Mme. A propos d'un cas de distomatose hépatique. [A Case of *Fasciola hepatica* Infection.] Bull. et Mém. Soc. Méd. Hôp. de Paris 1946 Nos. 1/2, 50-52.

The patient a man aged 30 was first treated in August 1942 for irregular vomiting and diarrhoea, without benefit. In January 1943 he was again examined and the diagnosis of infestation with *Fasciola hepatica* was suggested by blood examination which showed 67 per cent of eosinophiles, and was confirmed by finding the ova in the faeces.

He developed pleural effusion at this time associated with fever (40 C) on the first day but the temperature fell to 38 C next day before treatment with sulphonamides was begun and became normal a few days later. Lymphocytes formed 70 per cent of the cells of the pleural fluid and culture of the fluid remained sterile. The effusion meanwhile disappeared without any apparent involvement of the lung.

A week later (7th February) treatment with emetine was begun seven injections of 8 cgm. [ $1\frac{1}{2}$  grain] were ordered but by a mistake a single dose of 40 cgm. [6 grains] was injected and caused no untoward symptoms. Altogether he got 80 cgm. of emetine. Improvement was rapid the eosinophilia decreased to 31 per cent. in a few days and his weight increased by 2 kgm.

Six months later (August) treatment with stovarsol was begun [no mention is made of faecal examination] and the eosinophilia decreased to 8 per cent and in January 1944 it was 5 per cent. He was then given another course of emetine injections and recovered completely.

The author suggests that the pleural effusion was a pleural form of Loeffler's syndrome. The rapid improvement after the first course of emetine leads him to think that it might have been due to the large dose of emetine given by mistake. [For other references to infestation of man with *Fasciola hepatica* see this *Bulletin* 1942 v 39 14 703 1943 v 40 253 472 1944 v 41 677 1052]

J F Corson

ENWARDS C Cerebral Cysticercosis without Epilepsy *Lancet* 1946 Apr 6 500-501 1 fig on pl.

An airman aged 42 was invalided to England from the Azores after 5 months service in July 1944 because of two attacks of aphasia one in May and the other in June of that year. He had lived in the Middle and Far East from 1919 to 1925 and had since lived in England. In 1937 he developed a vague frontal headache which had been almost constantly present ever since. In 1942 he awoke one morning to find that the left half of his field of vision was impaired and this has since remained unchanged.

Medical examination in July 1944 showed incongruous homonymous hemianopic defects involving chiefly the lower left quadrant. No abnormality was seen by radiography of the skull. Lumbar puncture was done and the cerebrospinal fluid showed a pressure of 90-100 mm. of water and normal Queckenstedt test. There were no cells protein 0.07 per cent. a very slight increase in globulin, negative Wassermann reaction and the Lange gold curve was 443321000. The blood also gave a negative W.R. there were 8,300 white blood corpuscles and a differential count showed polymorphonuclears 60 per cent. lymphocytes 35 per cent. eosinophils 3 per cent., and monocytes 2 per cent.

On the 4th day after the lumbar puncture an irritable rash appeared on the thighs legs elbows and forearms and lasted for about 4 days.

On suspicion of a neoplasm being present the chest was radiographed and this disclosed the presence of numerous small calcified bodies in the muscles and subcutaneous tissues which were seen also all over the body. They were obviously cysticerci and careful search showed two subcutaneous nodules in the epigastric region and one in the left upper arm. An encephalogram was taken and showed short runs of waves with a frequency of 22 per sec. in both parietal regions. These interrupted a stable dominant frequency of 10 per sec. The disturbances which were numerous were considered to be epileptic in type. The patient was invalided from the Service his only symptom then being a slight headache.

The author notes that the incubation period (at least 12 years) is one of the longest recorded. DIXON and HARGREAVES [this Bulletin 1945 v 42 907] reported one of 20 years. Reference is also made to papers by MAC ARTHUR [this Bulletin 1934 v 31 334] and MARSH [*ibid* 788 see also ELSÄETER, *ibid.*, 1946 v 43 228] J F Corson

DICK, G W A. & MCCARTHY D D. The Absence of Anaemia in Hookworm Infestation in East African Personnel. *East African Med J* 1946 Jan v 23 No. 1 19-22. [19 refs.]

McCarthy [this Bulletin 1931 v 23, 21] made observations on natives in Pemba Island who had severe anaemia associated with hookworm infestation. The more heavily infested patients were treated with oil of chenopodium, iron and arsenic, as well as being given a full diet, while the less heavily infested patients were given a full diet extra eggs and fruit and 15 gm. of marmite daily but received no drugs. He concluded that the cause of anaemia associated with hookworm infestation was "an inadequate and probably deficient diet."

Dick made observations, recorded in the present paper, on 67 East African native soldiers in whose faeces hookworm ova were the only indication of the presence of pathogenic parasites (*Strongyloides stercoralis* and *Trichuris trichiura* were regarded as non-pathogenic). The controls were native soldiers with no evidence of any intestinal infestation. The observations consisted of erythrocyte counts and estimations of haemoglobin in the blood. The average number of erythrocytes (4.9 millions per cmm) was the same for the patients and the controls and the average haemoglobin content was slightly higher in the patients (101 per cent. or about 17 gm. per 100 cc.) than in the controls (99 per cent.).

The authors discuss the significance of their observations and conclude that hookworm infestation, unless it is very heavy, does not cause anaemia in East African natives who are well fed and are living under good conditions. When anaemia occurs it is due partly to deficiency of blood-building material (protein and iron) in the diet and partly to removal of blood by the hookworms. In such cases a good diet is more important than anthelmintics. J F Corson.

Cruz, W O & DE MELLO R. P. Profilaxia da anemia ancilostomótica. Síndrome da carencia. [Hookworm-Anaemia a Food Deficiency Syndrome. Its Prophylaxis.] *Mém. Inst. Oswaldo Cruz* 1945 Apr., v 42 No. 2 401-48, 11 graphs. [19 refs.] English summary.

[An account of an interesting series of experiments.] The fact has been observed that severe anaemia associated with ankylostomiasis occurs mainly in patients on a qualitatively insufficient diet, also that iron in the proper doses will cure the anaemia even though the worms persist. Further those who suffer from deficiency of iron in their diet are the ones to develop severe anaemia when they become infested with hookworm. On these grounds the suggestion is made to apply the administration of Fe salts in food prophylactically against hookworm anaemia, analogous to the use of iodide in the prevention of goitre. Hitherto the prophylaxis of ankylostomiasis and its associated anaemia has been attained by treatment of patients and the provision and use of latrines.

The end which the authors had in view was more difficult of attainment than the giving of iodide salt for goitre, for several reasons. Thus, the salt of Fe though in considerable quantity must not be such as to make the food unpalatable, the salt must remain stable for the time elapsing between mixing

with the food and partaking of the meal the colour of the food must not be so changed that contamination would be suspected the salt used ought to be haematologically active in small doses and it should be cheap and easily obtainable.

The authors tried 12 different salts of Fe the carbonate phosphate glycerophosphate, the sulphate the scale preparations and others added them to cooking salt to sugar to flour or meal noted the colour of the mixture the taste and the effect of therapeutic doses on the blood. The best was found to be ferrous sulphate mixed with meal or cooking-salt and with the latter of these there was considerable taste detectable so that the most efficient of all was the mixture with flour of manioc or cassava meal Another good mixture was Ferri et ammon cit with baked beans but this was more difficult in practice because the mixture changed the colour and it had to be very carefully prepared.

The dosage was usually Ferri sulph 1 gm. daily till the haemoglobin reached the normal level of 10-11 gm. per cent the therapeutic period then half this dose 0.5 gm. daily for some 80 days and after that 0.25 gm. for a like period the haemoglobin was thus maintained Then a vermifuge was given, 3 doses in 26-30 days or 4 doses in 40 days or so and the numbers of worms passed were counted. They might amount to several hundreds (717 in one case) Individual results are presented in graphs and tables.

H Harold Scott

YANG S C. H & LAUBE P J Biliary Ascariasis. Report of 19 Cases. *Ann Surgery* 1946 Feb., v 123 No 2 299-303

The authors review some of the literature which records the high incidence of ascariasis in man in China and elsewhere, yet the importance of biliary ascariasis is not sufficiently realized. MUTR [this *Bulletin* 1932 v 29 752] reported on a Chinese subject who had an ascarid in the common bile duct and he quotes 90 cases collected by AVILES [*Surg Gynecol & Obstet* 1918 Nov 459] from the literature up to 1918 and also 12 cases of biliary ascariasis detected at autopsy in the Philippine Islands. MORTON [*Arch. Surgery* 1928 v 17 324] reported one case from Virginia and eight others in the literature. CH'IN [*Chinese Med. J* 1933 v 47 1373] reported on a case of acute haemorrhagic pancreatitis due to *Ascaris* impacted in the ampulla of Vater and gave 28 references to biliary and pancreatic ascariasis. CH'IN [this *Bulletin* 1937 v 34 24] reported on a subject with ascariasis of the liver which caused fatal haemorrhage into the biliary tract and thence into the alimentary canal and peritoneal cavity CHEN [*Chinese Med. J* 1943 v 61A 51] reported three cases of biliary ascariasis one of which is the first now referred to by the present authors, who report on 19 cases seen in hospitals in Chengtu during the last 3 years.

All the present authors subjects complained of severe epigastric pain or pain in the right upper quadrant (one subject had pain in the epigastrium and left upper quadrant) The authors consider a distending pain more characteristic of biliary ascariasis than the stabbing kind of pain due to cholelithiasis. All but three of the patients vomited. The general symptoms suggested cholecystitis. Jaundice was present in five all but two had eggs of *Ascaris* in the stools. The temperature was low Ten of the patients had had similar attacks before. Three of them had cholecystitis four had distended gall bladders and five had tense firm common bile ducts, through the walls of which ascarids could be seen six had dilated bile ducts. Ascarids were present in the common bile duct of all Typically the anterior one-third



The author notes that the incubation period (at least 12 years) is one of the longest recorded. DIXON and HARGREAVES [this *Bulletin* 1945 v 42 907] reported one of 20 years. Reference is also made to papers by MAC ARTHUR [this *Bulletin* 1934 v 31 384] and MARSH [*ibid* 798 see also ELSAESSER, *ibid.*, 1946 v 43 228] J F Corson

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CRUZ, W O & DE MELLO R. P. Profilaxia da anemia ancilostomótica. Síndrome de carencia. [Hookworm Anaemia a Food Deficiency Syndrome. Its Prophylaxis.] *Mem Inst. Oswaldo Cruz* 1945 Apr v 42, No. 2, 401-48 11 graphs [19 refs.] English summary

[An account of an interesting series of experiments.] The fact has been observed that severe anaemia associated with ankylostomiasis occurs mainly in patients on a qualitatively insufficient diet: also that iron in the proper doses will cure the anaemia even though the worms persist. Further those who suffer from deficiency of iron in their diet are the ones to develop severe anaemia when they become infested with hookworm. On these grounds the suggestion is made to apply the administration of Fe salts in food, prophylactically against hookworm anaemia, analogous to the use of iodide in the prevention of goitre. Hitherto the prophylaxis of ankylostomiasis and its associated anaemia has been attained by treatment of patients and the provision and use of latrines.

The end which the authors had in view was more difficult of attainment than the giving of iodide salt for goitre, for several reasons. Thus, the salt of Fe, though in considerable quantity must not be such as to make the food unpalatable: the salt must remain stable for the time elapsing between mixing

with the food and partaking of the meal the colour of the food must not be so changed that contamination would be suspected the salt used ought to be haematologically active in small doses and it should be cheap and easily obtainable.

The authors tried 12 different salts of Fe the carbonate phosphate glycerophosphate the sulphate the scale preparations and others added them to cooking-salt to sugar to flour or meal noted the colour of the mixture taste and the effect of therapeutic doses on the blood. The best was found to be ferrous sulphate mixed with meal or cooking-salt and with the latter of these there was considerable taste detectable so that the most efficient of all was the mixture with flour of manioc or cassava meal. Another good mixture was Ferri et ammon. cit with baked beans but this was more difficult in practice because the mixture changed the colour and it had to be very carefully prepared.

The dosage was usually Ferri sulph 1 gm. daily till the haemoglobin reached the normal level of 10-11 gm per cent the therapeutic period then half this dose 0.5 gm. daily for some 80 days and after that 0.25 gm. for a like period the haemoglobin was thus maintained. Then a vermifuge was given 3 doses in 26-30 days or 4 doses in 40 days or so and the numbers of worms passed were counted. They might amount to several hundreds (717 in one case) Individual results are presented in graphs and tables

H Harold Scott

YANG S C H. & LAUBE P J Biliary Ascariasis. Report of 19 Cases. *Am. Surgery* 1946 Feb., v 123 No 2 299-303

The authors review some of the literature which records the high incidence of ascariasis in man in China and elsewhere yet the importance of biliary ascariasis is not sufficiently realized MUIR [this *Bulletin* 1932 v 29 752] reported on a Chinese subject who had an ascari in the common bile duct and he quotes 90 cases collected by AVILES [Surg Gynecol & Obstet 1918 Nov 459] from the literature up to 1918 and also 12 cases of biliary ascariasis detected at autopsy in the Philippine Islands. MORTON [Arch Surgery 1928 v 17 324] reported one case from Virginia and eight others in the literature. CHEN [Chinese Med J 1933 v 47 1373] reported on a case of acute haemorrhagic pancreatitis due to *Ascaris* impacted in the ampulla of Vater and gave 28 references to biliary and pancreatic ascariasis. CHEN [this *Bulletin* 1937 v 34 24] reported on a subject with ascariasis of the liver which caused fatal haemorrhage into the biliary tract and thence into the alimentary canal and peritoneal cavity CHEN [Chinese Med J 1943 v 61A 51] reported three cases of biliary ascariasis one of which is the first now referred to by the present authors who report on 19 cases seen in hospitals in Chengtu during the last 3 years

All the present authors subjects complained of severe epigastric pain or pain in the right upper quadrant (one subject had pain in the epigastrium and left upper quadrant) The authors consider a distending pain more characteristic of biliary ascariasis than the stabbing kind of pain due to cholelithiasis All but three of the patients vomited. The general symptoms suggested cholecystitis Jaundice was present in five all but two had eggs of *Ascaris* in the stools The temperature was low Ten of the patients had had similar attacks before Three of them had cholecystitis four had distended gall bladders and five had tense, firm common bile ducts through the walls of which ascari could be seen six had dilated bile ducts Ascari were present in the common bile duct of all Typically the anterior one-third

of an ascariid 20 cm. long, projected into one of the hepatic ducts, the remaining part of the nematode extending down the common bile duct to the duodenum. In three subjects there were ascariids either partly or completely in the gall bladder as well as in the common bile duct.

The authors comment on the predilection of *Ascaris* to enter any available opening. They have been found projecting through holes in swallowed glass beads or buttons and in the appendix if no openings are available, they burrow into tissues. More serious consideration should be given to biliary ascariasis. If, in an area in which *Ascaris* is endemic, a young person below the usual age for cholelithiasis shows symptoms of disease of the biliary tract, biliary ascariasis should be suspected. This diagnosis is reasonable if the stools contain eggs of *Ascaris* if there is a recent history of ascariasis, if ascariids have been vomited recently if there is a history of similar previous attacks and if the subject has the characteristic peculiar distending pain. [See also GUHL, this Bulletin 1945 v 42 51] G Lafage

ASHBURN L. L. PERRIN T. L. BRADY F. J. & LAWTON A. H. Histologic Changes in Ovary and Uterus of Live *Dirofilaria immitis* recovered from Dogs treated with Trivalent Antimony Compounds. Arch Pathology 1945 Nov-Dec v 40 No. 5 334-8 2 figs

We have little knowledge of the effects upon nematodes of drugs used for the treatment of infestations with them. The authors treated dogs infested with *Dirofilaria immitis* with antimonial and mercurial compounds and studied histologically the effects of these drugs upon the ovaries, and upon the developing ova and microfilarial larvae in the uteri of the nematodes.

IZAGAMI and MAKINO [this Bulletin 1927 v 24 995] noted that there were no embryos in the uteri of worms recovered from the heart of one dog eight and a half months after it had been treated with sodium antimonyl tartrate. WRIGHT and UNDERWOOD (J. et. Med. 1934 v 29 234) found no embryos in the uteri of adult worms removed from dogs killed after the 37th day of treatment with Fouadin. WRIGHT and HARWOOD [see CHRISTIE, this Bulletin 1944 v 41 139] state that some observations indicate that the sterilization of female *Dirofilaria immitis* was due to fatty degeneration and necrosis of the reproductive cells of the ovary. [They also summarize our knowledge of the mode of action of anthelmintics.] BROWN and SHELTON (ibid 1942 v 39 190) could not find microfilarial larvae in the uteri of female nematodes recovered alive from dogs treated with a combination of Fouadin and sulphamylamide. LAWTON et al (ibid 1946 v 43 55) report the elimination of circulating microfilarial larvae by 23 out of 24 trivalent antimonial compounds and the failure of mercurial compounds in this respect.

The present authors examined specimens of *D. immitis* recovered from 25 dogs treated with various antimonial compounds and from two dogs treated with mercurial compounds. [No list of these compounds is given.] Microfilarial counts were made from samples of the blood of the dogs each time the drugs were given (6 days a week). As controls 15 female *D. immitis* were used 10 being obtained from five untreated dogs and 5 from two dogs which died 2½ hours after a single dose of one of the drugs being tested. The worms were wound round glass tubing and the ends fixed with rubber bands. They were then fixed in 10% solution of formaldehyde U.S.P. The nematodes were dehydrated in acetone cleared in benzene and cedar oil and embedded in 56°C. paraffin wax. The stains used were haematoxylin azure eosinate [see LILLIE, Stain Technology 1941 v 16 1] and van Gieson's stain. All the descriptions given refer to the posterior ovaries anterior ovaries were never

seen. For the details of the appearances seen, the paper and its illustrations must be consulted.

It was evident that at least temporary sterilization of female *Dirofilaria* could be accomplished by treatment of their hosts with antimonial compounds. Eight sterilized *Dirofilaria* were obtained from eight dogs treated with these compounds 70 to 107 days after completion of treatment. Longer observation is required to determine whether the sterilization of *Dirofilaria* is permanent. BROWN [this *Bulletin* 1945 v 42, 53] found that treatment of patients with lithium antimonyl tartrate reduced the microfilarial count 85 to 100 per cent in 4½ to 5 months and thought it likely that the filarial nematodes had been killed. The present authors however think it likely that the nematodes were sterilized for they found females of *Dirofilaria immitis* which were sterilized 3½ months after the end of the treatment. Such a result would be valuable because it would reduce the degree of infestation of the mosquito intermediate hosts. The authors think that although direct action of the drugs on the microfilarial larvae and on multicellular ova may have caused the absence of these developmental stages it is more likely that the drug acted directly on the earlier stages of development so that the microfilarial stage was never reached. The presence of degenerate ova in the uterus of some *Dirofilaria* up to 107 days after treatment of the dogs had ceased is not likely to have been due to persistence of the necrotic material for so long some of these degenerate cells had retained their form which suggests that their degeneration had been recent. The authors therefore suggest that although the ova were shed into the uterus they had been injured so much that they could not develop or that the worms retained the drug so long that the ovaries were influenced by it for some time after treatment ended.

Thus the therapeutic compounds used caused changes in the ovary, the developing ova and microfilarial larvae which agreed well in most instances with the microfilarial counts of the circulating blood. The changes seen were early degeneration or necrosis of the ova and the absence of microfilarial larvae from most of the females. The uterus of some females were entirely empty and there were areas of necrosis in their ovaries. The worms taken from two dogs treated with mercurial compounds were normal. G Lapage

WILLIAMS R. W. & BROWN H. W. The Transmission of *Litomosoides carinii* Filarid Parasite of the Cotton Rat, by the Tropical Rat Mite, *Liponyssus bacoti*. *Science* 1946 Feb 22 224

Cotton rats *Sigmodon hispidus* infected with the filarial worm *Litomosoides carinii* were kept separately in cages in boxes and tropical rat mites *Liponyssus bacoti* were added to infest the rats and multiply on them. Two white rats in separate cages were afterwards placed in the boxes alongside the cages of the cotton rats and became infected with the filaria. Control white rats similarly placed near infected cotton rats but in the absence of the mites did not become infected with the filaria. It was concluded that the tropical rat mite serves as a vector of this worm.

Adult *L. carinii* were found in the pleural cavity of the white rats after 42 and 44 days respectively. In one rat the worms were from 1.165 mm. to 1.2 mm. long in the other rat they were 9 mm. and 42 mm. The control rats were negative when examined at 44 days.

In the infective stage in the mites the worms are from 800µ to 1 000µ in length and it is interesting that a worm only 163µ longer than the biggest worm in a mite was found in the pleural cavity of one of the white rats. This suggests either that the worm reaches the pleural cavity very quickly or that it grows very slowly before reaching the pleural cavity.

Microfilariae were seen in the blood of both cotton and white rats, experimentally infected by mites, after 80 days and it is thought that they may appear as early as 50 or 60 days after exposure to infection. J F Corson

GOLDMAN L. & ORTIZ L. F. Types of Dermatitis in American Onchocerciasis. *Arch. Dermat. & Syph.* 1946 Feb., v 83 No. 2, 79-83 7 figs.

A description of some of the forms of dermatitis found in association with onchocerciasis in Chiapas, Mexico a district where the endemicity of the disease is high. There are difficulties in deciding what forms are due actually to *Onchocerca* infestation and what to associated conditions, such as pruritus from mycotic infections, pinta, tropical ulcers, syphilis etc.

The authors first give a list of 'cutaneous reactions' observed in patients with onchocerciasis and this includes scarring from cutaneous biopsies or excision of nodules and "dermatitis from therapeutic agents" neither of which could strictly be called dermatitis in onchocerciasis nor could reactions to the bite of simuliid which might or might not be carrying *Onchocerca*. They then describe in detail three forms of dermatitis definitely associated with onchocerciasis, namely the pigmentation dermatitis or *mal de morado* (purple disease) a lichenoid form, and an eczematoid dermatitis.

In the first of these the skin may be dry or wrinkled, but is usually smooth, of a bluish-red or purple (morado) colour perhaps with local oedema. Biopsy reveals microfilariae in the upper part of the dermis. Most of those with this condition have previously had onchocerca nodules. It may be associated with pruritus and oedema. The face is often involved and puffiness with oedema and cosmophyllia are reminiscent of trichinosis.

The second or lichen type chiefly affects the face and may occur with the third type (see below) but may also affect the arms and less often the legs. The skin is thickened and hyperpigmented, and there is intense itching. Biopsy reveals microfilariae in the pars papillaris. In the third, the eczematoid type there are papulo-vesicular excoriated lesions sometimes impetiginous or there may be papulomatous verrucose and hyperkeratotic patches on arms, hands and neck.

Treatment of these conditions comprises removal of onchocerca swellings (onchocercomas) and local treatment of the cutaneous condition on the usual lines.

H. Harold Scott.

### DEFICIENCY DISEASES.

MUKELMAN M. M. Nutritional Diseases in Cebu. *War Medicine* Chicago 1945 Nov.-Dec. v 8 No 5 325-32.

This is a straightforward account of the experiences of a U.S. army doctor imprisoned by the Japanese in the Philippines. Rations were short during the period of resistance on the Bataan peninsula, and after surrender in April 1942, the ration allowed consisted of about 300 gm. rice, 30 gm. flour, 10 gm. sugar, 10 gm. oil and 100 gm. leaves and stems of vegetables or vines, with occasionally about 5 gm. of carabao meat. This diet provided less than 1,500 calories, less than 30 gm. protein, and very small amounts of vitamins.

Swollen ankles were noted early in many of the men, while some had generalized oedema. Soon 25-50 per cent. had symptoms of beriberi with neuritis and oedema. Signs of pellagra took longer (4-8 months) to appear but then progressed rapidly. A home-grown culture of yeast was prepared in sufficient quantity to ameliorate the symptoms of the worst sufferers, but was insufficient to produce cure.

By late October 1942 90 per cent of the prisoners suffered from malnutrition, and fully 50 per cent were seriously ill with beriberi pellagra malaria, dysentery or other infectious diseases. The fever anorexia, digestive disturbances and diarrhoea associated with these latter diseases contributed to the deficiency states. Symptoms of optic neuritis appeared in over half the prisoners while cerebral spinal and peripheral nerve lesions gave many variations to the clinical picture.

The arrival of Red Cross supplies was followed by an improvement in the diet, and in most cases by a rapid improvement in the physical condition of the prisoners. The ending of these extra supplies was marked by a return to the previous deficiency states again alleviated by a fresh supply while this lasted.

In the summer of 1944 men doing hard labour were issued with food supplying less than 1 000 calories a day while the remainder received less than 800 calories. After this extreme reduction many men were seen to have attacks of hypoglycaemia.

In the autumn of 1944 after a widespread epidemic of dengue about a third of the 500 men in one camp showed a symptom complex similar to myasthenia gravis. Its aetiology and nature were never clearly defined and the condition tended to disappear.

After release of the prisoners from captivity and their return to a full diet, the gain in weight the clearing of pellagrous lesions the loss of oedema and the improvement in the neurological lesions were remarkable. It is felt however that complete recovery is unlikely in patients with advanced nerve lesions.

Scurvy never constituted a serious problem. A long delay in the healing of wounds was an embarrassing surgical problem that may have been determined in part by subclinical scurvy.

*H E Harding*

MUSSELMAN M M Pellagra in Americans in a Japanese Prison. *Bull US Army Med Dept* 1946 Apr v 5 No. 4 403-11

After 6-7 months on a diet affording less than 1,500 calories less than 30 gm. of protein most of which was of vegetable origin and very small amounts of vitamins pellagra was observed in rapidly increasing numbers of prisoners. Within a short time almost every prisoner showed some signs of the condition while half of them had fairly severe lesions of the mouth and skin. Administration of a thin culture of air borne yeasts was of marked therapeutic value but the quantities available allowed treatment of only the more severe cases.

After the receipt of Red Cross supplies the general condition improved markedly only to relapse with the exhaustion of these supplements. It was noted that pure preparations of vitamins were more effective when the diet was more adequate.

[See also paper by MUSSELMAN above.]

*H E Harding*

SOUTH AFRICAN RED CROSS SOCIETY (NATAL BRANCH) Report to the Red Cross Society, Natal, on an Experiment with Pre-Digested Protein [DORMER B. A.] 20 pp 8 charts & 15 pls

Dr Dormer reports that the death rate from tuberculosis has risen from 250 to 700 per 100 000 in some industrial areas of South Africa during the war and he also finds a great increase in severe oedema in native children and in frank nutritional deficiency diseases in adults. Much of this increase he believes is connected with a lowered standard of nutrition and in particular with a lessened intake of protein.

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of these acids with polypeptides, peptones, etc. Whale flesh is commonly almost completely wasted and large amounts of it could be made available in this manner. The products are bitter and unpalatable but their taste can be disguised in soups, wines, chocolates, toffees and biscuits.

Experimental trials of these products have given very favourable impressions to their users. Patients with pulmonary tuberculosis who were previously losing weight steadily, have in most cases gained weight, and their general condition has improved. Similar results have been obtained in a few patients with tuberculous enteritis. It is not claimed that feeding with these mixtures is a cure for tuberculosis, but the improvement produced in the patient's condition sometimes allows active therapy to be undertaken.

Native children suffering from malignant oedema or infantile pellagra have shown rapid improvement when treatment is started with these products and glucose. Tropical ulcers have been found to heal rapidly. Feeding with these protein digests is also recommended for patients with peptic ulcers, nephrosis, hepatitis, diabetes, hyperthyroidism, anorexia nervosa, and various allergic states.

[This is a report to the South African Red Cross Society urging an extension of the support given to Colonel Watkins Pitchford. It is not meant to be a properly documented scientific report. Judged, however, on the very lowest level it does draw attention to the very serious effects of malnutrition in South Africa, and it points to a hitherto untapped source of protein.]

H. E. Harding

GILLMAN J. MANDELSTAM, J. & GILLMAN T. A Comparison of Chemical and Histological Estimations of the Iron and Copper Content of the Livers of Africans in relation to the Pathogenesis of Cytochromosis and Cirrhosis (Haemochromatosis). *South African J. Med. Sci.* 1945 Dec. v 10 No. 4 109-36 7 figs. on 1 pl. [80 refs.]

A comparison of the amount of iron assessed by histological methods and that found by chemical analysis in 73 livers showed fairly good correlation. It was found that iron might be visible histologically without any increase in the quantity found chemically i.e. that normally bound and invisible iron could become visible. Livers from pellagra were classified in four types [GILLMAN and GILLMAN this *Bulletin* 1946 v 43 364]. On the whole this typing was found to correspond with increasing quantities of iron determined chemically but there was considerable overlap between individual livers in each group.

Cirrhosis and pigmentation are separate conditions. Extensive cirrhosis may exist without a significant increase in the amount of iron. Iron may be present in quantities as great as those described in haemochromatosis without any cirrhosis. Cirrhosis may be found with very varying quantities of iron which may be in liver cells only or in the portal tracts as well.

The amount of copper in the liver does not vary directly with the amount of a marked increase in the latter there is usually an increase in

} quoted in the text Sheldon's book.—Haemochromatosis does not appear in the list of references.)

H. E. Harding

of Nutritional  
Nov-Dec

to Cardiac Dysfunction  
No. 5 341-8 [Refs. in

followed by a summary  
changes in pigs given a

diet deficient in thiamin. In these animals thiamin deficiency leads to severe changes in cardiac function, and produces well defined histological lesions. It is still undecided whether a deficiency of thiamin produces similar changes in man. The lesions found in pigs are unlike those that have been described as occurring in the heart in beriberi and resemble more those that have been described under the title of isolated myocarditis or Fiedler's myocarditis.

H E Harding

## SPRUE.

BLACK D A K. FOURMAN L P R. & TRINDER, P. Fat-Absorption in Tropical Sprue. *Lancet* 1946 Apr 20 574-5

[A piece of work of no little importance to those interested in the study of the problems of sprue.] The authors have carried out experiments to determine the degree of fat-absorption in sprue at an early stage. All the patients suffered from steatorrhoea and had lost weight some had glossitis and showed signs of macrocytic anaemia. The percentage of fat-absorption was determined by the formula

$$\frac{(\text{Dietary fat} - \text{excreted fat}) \times 100}{\text{Dietary fat}}$$

In untreated patients with sprue in various stages but with formed stools the absorption ranged between 51 and 83 per cent., with an average of 75.8 per cent. three others with watery diarrhoea, had generally a lower absorption 30.55 and 64 per cent. In the cases of five patients the fat content of the diet was raised by about 40 per cent. from 69 to 96 gm. a day. As a result more fat was excreted but there was little change in the proportion absorbed in two it remained practically the same (82 and 85 in place of 83 and 87 per cent.) in one it rose slightly (83 to 88) in two it fell (from 80 and 51 to 74 and 44 respectively). The natural inference is that moderate increase in dietary fat has little effect on absorption.

Giving nicotinic acid, riboflavin or pantothenic acid did not improve the absorption. The effect of liver is more remarkable though the stomatitis and glossitis improved and weight was gained fat absorption was not affected unless there was diarrhoea in such patients improvement of the diarrhoea was accompanied by increased fat-absorption. Giving of a yeast extract of the Marmite type seemed to increase fat-absorption this may be due to its folic acid content. The question is to be the subject of further study.

From the investigations so far carried out the following points emerge (1) Intestinal secretion of fat does not play an important part in causing steatorrhoea for the latter disappears on a very low fat diet. (2) Sprue is not due to diminished motility of the villi or reduced absorptive surface because the absorption percentage remains almost constant when the intake of fat is moderately increased. (3) This constancy is more easily explained by theories based on the failure of an enzyme system such as that concerned in phosphorylation. [See STANNUS this Bulletin 1943 v 40 259]

H Harold Scott.

DARBY W J JONES E. & JOHNSON H C. The Use of Synthetic *L. casei* Factor in the Treatment of Sprue. *Science* 1946 Jan. 25 108.

DAY *et al* (*J Biol Chem* 1945 v 157 423) showed that vitamin M deficiency in the monkey is promptly cured by the injection of purified *Lactobacillus casei* factor and thus led the authors of this paper to try synthetic *L. casei* factor (Lederle) (1)<sup>2</sup> in the treatment of three cases of sprue

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GILLMAN J. MANDELSTAM J. & GILLMAN T. A Comparison of Chemical and Histological Estimations of the Iron and Copper Content of the Livers of Africans in relation to the Pathogenesis of Oxydokeroids and Cirrhosis (Haemochromatosis). *South African J. Med. Sci.* 1945 Dec. v 10 No. 4 109-38 7 figs. on 1 pl. [60 refs.]

A comparison of the amount of iron assessed by histological methods and that found by chemical analysis in 73 livers showed fairly good correlation. It was found that iron might be visible histologically without any increase in the quantity found chemically i.e. that normally bound and invisible iron could become visible. Livers from pellagrins were classified in four types [GILLMAN and GILLMAN this *Bulletin* 1946 v 43 364]. On the whole this typing was found to correspond with increasing quantities of iron determined chemically but there was considerable overlap between individual livers in each group.

Cirrhosis and pigmentation are separate conditions. Extensive cirrhosis may exist without a significant increase in the amount of iron. Iron may be present in quantities as great as those described in haemochromatosis without any cirrhosis. Cirrhosis may be found with very varying quantities of iron, which may be in liver cells only, or in the portal tracts as well.

The amount of copper in the liver does not vary directly with the amount of iron, but with a marked increase in the latter there is usually an increase in the former.

[Although frequently quoted in the text Sheldon's book—Haemochromatosis, Oxford 1935 does not appear in the list of references.]

H. E. Harding

WINTROBE M. M. Relation of Nutritional Deficiency to Cardiac Dysfunction. *Arch. Intern. Med.* 1945 Nov-Dec. v 78, No. 5 341-6. [Refs. in footnotes.]

A brief review of the literature on cardiac beriberi is followed by a summary of the work at the University of Utah on the cardiac changes in pigs given a

cent whereas among 30 Mongoloid and 120 Caucasoid individuals no example of sicklaemia was found

In 58 sicklaemic persons with morbid conditions producing circulatory stasis anatomico-pathological changes of sickle cell anaemia were not observed. These findings contradict the hypothesis that stasis is a sufficient factor for the transition from a sicklaemic to an anaemic condition. In 13 sicklaemic persons infected with malaria no symptoms of sickle cell anaemia were observed, but it was also verified that parasitism by *P. vivax* does not check sickling.

It is important when determining sicklaemic indices to take into consideration the direct hereditary factor as the index for a familial group may be much larger than that obtained by random sampling to differentiate the familial incidence the term familial sicklaemia index is suggested. Sickle cell anaemia may only be obvious at times in generations very distant one from another giving rise to a skipping phenomenon in such cases the condition is maintained in the intervals through sicklaemic individuals who may be regarded as potentially diseased or as healthy carriers of a pathogenic feature.

The systematic and periodical examination of sicklaemic individuals is urged as such investigations may throw light on the genetically transmitted factors and also on the intrinsic and extrinsic factors associated with the disease. Control of the condition would also be aided by a census of sicklaemic individuals and remarks on their identification cards by the systematic examination for sicklaemia of all the newly born by the supervision of all sicklaemic individuals who should be required to present themselves to the public health authorities periodically and especially on the appearance of any symptoms of the disease and finally by the inclusion of tests for sicklaemia in prenuptial medical examinations.

F Murgatroyd

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## VENOMS AND ANTIVENENES

MARTIN W B Clinical Experience with Snake Bites on Okinawa. *Bull U.S. Army Med Dept* 1946 Jan v 5 No 1 79-82

Nine cases of snake bite which occurred during the Okinawa campaign are described. Four case reports are given in full. In all instances in which the snake was identified it was the Habu (*Trimeresurus flavoviridis*). There were no fatalities. Clinically there was a rapid onset of symptoms with brief local anaesthesia in some cases followed by pain and swelling and systemic disturbance. The venom was mainly haemotoxic and had no effect on the brain centres.

Treatment recommended includes criss-cross incisions over the site of the fang marks suction immediately and intermittently for 12 hours and if the bite is in a limb the application of a tourniquet tight enough to prevent venous return but not enough to compress the arteries and it should be released every 20 minutes and replaced at higher levels if the swelling is progressing proximally. The authors advise the administration of Nearctic antivenene although none of their cases was treated in this way. Penicillin should be given in doses of 20 000 units 3-hourly (after an initial dose of 30 000 units) in view of the penetrating wound and local oedema.

[No mention is made of washing the site before the incision in order to remove ejected venom.]

B G Macgrath

Crystalline synthetic *L. casei* factor was dissolved in water with a small quantity of disodium phosphate, and the solution was autoclaved 15 mgm. of the factor in this solution were injected intramuscularly daily. Improvement both clinical and haematological followed rapidly in all three patients: the symptoms of glossitis disappeared within 3 or 4 days and the lingual papillae were regenerated; the diarrhoea ceased, the appetite improved and the body weight increased, one patient gaining 26 lb in the first 6 weeks. There was a great increase in the numbers of reticulocytes, blood platelets and blood leucocytes, and some increase also of haemoglobin and of erythrocytes: sternal puncture showed improvement in the bone marrow.

This striking response to the treatment suggested to the authors certain possible relationships: the synthetic *L. casei* factor is probably identical with, or closely related to, the substance in liver extract which is effective in the treatment of sprue, this syndrome and that of vitamin M deficiency in the monkey being similar (LANGSTON *et al* *J Exper Med* 1938, v 68, 923) since the factor which relieves the macrocytic anaemia of pregnancy is closely allied to vitamin M, the synthetic *L. casei* factor may be efficacious in the treatment of that form of anaemia: the *L. casei* factor may be related to the erythrocyte maturing factor since in sprue and pernicious anaemia the blood picture, the bone marrow and the glossitis are similar.

SPIES *et al* (this *Bulletin* 1946 v 43 375) found that synthetic *L. casei* factor was effective in the treatment of incompletely diagnosed macrocytic anaemia and GOLDSMITH (personal communication) reported the successful treatment of "nutritional macrocytic anaemia with folic acid".

The authors' references include also DAY (in *Vitamins and Hormones* ed. by HARRIS and THOMAS 1944 New York, Acad Press Inc v 2, 71) WILLS and STEWART (*Bulletin of Hygiene* 1936 v 11 186) [Other references to macrocytic anaemia are: this *Bulletin* 1938 v 35 846 1939 v 36 422 1940 v 37 863-5 1941 v 38, 184 1942 v 39 482, 483 1943 v 40 405 484 838 1945 v 42, 59 222, 308, 482 1946 v 43 146.]

J. F. Corson

## HAEMATOLOGY

DA SILVA E. M. Estudos sobre índice de sickleia [Studies on the Sicklaemia Index.] *Mem Inst Oswaldo Cruz* 1945 Apr v 42 No 2 315-40 10 figs [47 refs.] English summary.

The sickle cell trait may be detected by several well-known methods. For a rapid determination, the blood may be exposed to a current of carbon dioxide. For large scale surveys coverglass preparations of either fresh blood or blood mixed with an isotonic anticoagulant solution are useful. The addition of anti-A or anti-B agglutinating serum does not check sickling so that by such combinations the blood group and the sickle cell trait may be determined at the same time. Similarly, the addition of solutions of brilliant cresyl blue may be used for the simultaneous determination of the degree of reticulocytosis and the sicklaemia. For the study of the process of sickling mixtures of blood and isotonic anticoagulant may be sealed in tubes and sampled at intervals, the cells being fixed by the addition of formalin at the time of sampling. Finally, maceration in isotonic saline or fixative solutions, of tissues preserved in alcohol or formalin, may enable a retrospective determination of sicklaemia to be made after a period as long even as 26 years.

Among a heterogeneous group of 1130 negroes and negro cross-breeds 113 sicklaemic individuals were found, giving an index of approximately 10 per

increasing prostration and death in 3 to 40 hours. With guineapigs large doses to 185 gm. subcutaneously were needed to produce these symptoms and a local saccular oedema occurred. 80 mgm. intramuscularly caused redness and swelling but was not fatal. In rabbits 50 mgm. intravenously caused death in 15 minutes. In pigeons 6-8 mgm. intravenously killed in 10 minutes or less but as much as 125 mgm. were needed intramuscularly or subcutaneously to kill in 10 minutes by the former route in 4-12 hours by the latter.

*Opisthophthalmus* venom. 2-3 mgm. were needed intravenously to kill mice in 1-20 minutes the symptoms of excitability, dyspnoea and paralysis resembling those with the other venoms. Subcutaneous and intramuscular injections in doses of 20-80 mgm. in guineapigs differed from the other venoms in producing severe local haemorrhagic swelling, gelatinous oedema and later sloughing the same occurred in pigeons. These routes were not tried with rabbits.

As regards haemolysis this effect occurred with all the venoms but only in relatively high concentrations such as 20 mgm. per cc. guineapig erythrocytes were haemolysed more readily than sheep's cells and the haemolysis was less marked with *Parabuthus* venom than with either of the others.

The effects of heat were observed, at 70°C in a water-bath for  $\frac{1}{2}$  hour at boiling point for 30 minutes and for 90 minutes the toxicity of the venoms remained practically unchanged. In high concentration of 10-30 mgm. per cc. the *Parabuthus* venom had a graded proteolytic action on gelatin *in vitro* the other two had no such action.

Tests with antivenenes of *Naja ferox* and *Buthus ardens* showed them to be ineffectual against these scorpion venoms. Preparation of specific antiscorpion serum from horses was undertaken starting with toxoid and continuing with natural venom. Practitioners were asked to report on the results of the use of these antivenenes and so far though only a few reports have come in, they appear to be favourable when the serum is injected intramuscularly in a dose of 10 cc.

H. Harold Scott

TINKHAM E. R. A Poison-Squirting Spider *Bull U.S. Army Med Dept*  
1946 Mar v 5 No 3 361-2.

A soldier in Florida, U.S.A. while inspecting the tail lamp of his motor cycle one day at noon, saw a spider about 12 to 15 in. distant and disturbed it at that moment he felt something enter his eye and it caused him great pain. His eye became inflamed, conjunctivitis persisting for two days. He thought the spider had squirted something from its mouth into his eye, while another soldier who was present thought it had squirted from its abdomen. The spider was caught and was identified as *Peucedan* the identification being confirmed afterwards from the author's drawings and description, by H. J. GERTSCH arachnologist American Museum of Natural History New York who however stated that this species was not known to squirt venom and that he knew of no other spider with that reputation except perhaps *Scytodes* which captures its prey by spitting on it from a short distance.

J. F. Corson

ARANTES, J. B. KARMAN, G. & BIER, O. G. Emprego da reacção de floculação específica na dosagem do antiveneno crotálico. [Applicability of the Specific Flocculation Reaction for the *in vitro* Titration of Crotaline Antivenoms.] *Mém. Inst. Butantan*. 1944-1945 v 18, 21-6. English summary (7 lines)

BIER, O. G. Estudo quantitativo da reacção de floculação entre o veneno e o antiveneno crotálico. [A Quantitative Study of the Flocculation Reaction between the Venom of *Crotalus i. terrificus* and its Specific Antivenom.] *Mém. Inst. Butantan*. 1944-1945 v 18, 27-32. English summary (8 lines)

GRASSET, E. SCHAAFSMA, A. & HODGSON, J. A. Studies on the Venom of South African Scorpions (*Parabuthus Hadogenes Opisthophthalmus*) and the Preparation of a Specific Anti-Scorpion Serum. *Trans Roy Soc Trop Med & Hyg*. 1946 Apr v 39 No 5 397-421 3 figs. on 2 pls. [19 refs.]

In South Africa, cases of scorpion sting are not infrequent but, as elsewhere where scorpions abound, fatalities are rare and occur mostly in children. Much work has been done on the taxonomy and systematics of South African scorpions but little on their relative toxicity. The authors in this paper record their investigations on three genera. *Parabuthus* especially *P. transvaalicus* and *P. irradians* from the northern Transvaal and Bechuanaland; this genus is common throughout Africa and Arabia but is not found in Natal and Pondoland. *Hadogenes* especially *H. troglodytes dentatus* found in South Africa, Portuguese East Africa, the Congo and Madagascar but not along the coast from Capetown to Port Elizabeth. *Opisthophthalmus* especially *O. walberghi* and *O. glabrifrons* from Bechuanaland.

For experiment venom was obtained from *Parabuthus* by aspiration with a pipette after the tip of the telson had been cut from the others, which had more delicate telsons, by squeezing out with forceps. In each case, the venom, a white milky fluid, was collected on a watch-glass and allowed to dry. The average yields of dried venom for each scorpion were *Parabuthus* 4.8 mgm. *Hadogenes* 2.7 mgm. *Opisthophthalmus* 1.4 mgm.

For their experiments the authors prepared saline solutions standardized to contain 10 mgm. per cc. and the animals used were mice, guinea-pigs, rabbits and pigeons. Injections were made intravenously, subcutaneously, intramuscularly, intracutaneously and intracerebrally. In solution the venoms are unstable, so all experiments were made with freshly prepared solutions. The results were as follows:—

*Parabuthus* venom. White mice average weight 22 gm. 0.1-0.4 mgm. intravenously caused immediate dyspnoea, staggering and inco-ordination, extension of hind legs, or gasping uncontrolled jumping and paralysis; death occurred in  $\frac{1}{2}$  to 5 minutes with progressive paralysis and asphyxia. Subcutaneously the symptoms were similar but the dose needed was four times the intravenous dose. 0.002-0.1 mgm. intracerebrally produced immediate convulsions, trembling, paralysis and death in a few seconds with the larger dose. In other animals the symptoms were similar. The dosage for guinea-pigs of 350-400 gm. was 1-2 mgm. subcutaneously or intramuscularly; for rabbits of 2,000 gm. 5 mgm. intravenously; in pigeons of 400-450 gm., with 0.8-1.5 mgm. intravenously there were marked neuromotor symptoms. To epitomize *Parabuthus* venom is neurotoxic producing at first neuromuscular excitability and dyspnoea from action on the respiratory centre, followed by paralysis and asphyxia.

*Hadogenes* venom. 0.4-0.6 mgm. intravenously in mice caused dyspnoea and paralysis, and death within 15 minutes. Subcutaneously large doses, up to 40 mgm., produced hyperexcitability for 1-2 hours, then trembling and

increasing prostration and death in 3 to 40 hours. With guineapigs large doses to 185 gm subcutaneously were needed to produce these symptoms and a local saccular oedema occurred. 80 mgm. intramuscularly caused redness and swelling but was not fatal. In rabbits 50 mgm. intravenously caused death in 15 minutes. In pigeons 6-8 mgm. intravenously killed in 10 minutes or less, but as much as 125 mgm. were needed intramuscularly or subcutaneously to kill in 10 minutes by the former route in 4-12 hours by the latter.

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H Harold Scott

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J. F. Corson



## DERMATOLOGY AND FUNGUS DISEASES

VARELA, G. Estudios serológicos y cardiovasculares de un grupo seleccionado de enfermos de mal del pinto. [Serological and Cardiovascular Studies on Pinta Patients.] *Rev. Inst. Salubridad y Enfermedades Trop. Mexico*. 1945 Sept., v 6 No 3 163-6.

Twenty-nine patients suffering from mal del pinto whose ages ranged between 4 and 20 years were selected because they had not received any treatment for their disease and gave no history of having been infected with syphilis. Tests were made with their sera and cerebrospinal fluids for complement fixation, and the reactions of Pandy, Nonne-Apel't and Mazzini were carried out with the cerebrospinal fluids. Radiograms were taken of the heart and electrocardiograms made.

Some previous investigators have recorded positive results with the c.s.f. for example, the Mexican Commission on Pinta in 1930 (number of cases not stated) reported Wassermann reactions markedly positive. PARDO CASTELLO in 1936 recorded 4 out of 26 as having an increase in globulin and one with a positive Wassermann reaction and positive Kahn. GRAU and TRIANA in 1937 recorded two positive out of 12. On the other hand, BOTERO in 1939 and León BLANCO in 1942 found no change in the fluid of 69 and 53 patients respectively. The present author's investigations support the last named. The sera in all his patients gave a marked positive reaction but the cerebrospinal fluids were without exception negative. The electrocardiograms also showed no departure from the normal though three showed by X rays an increased area of the aorta. *H. Harold Scott*

DONES, W. L. & JONES, J. Erythema Streptogenes. *Arch. Dermal & Syph.* 1946 Feb., v 53 No. 2 107-14 4 figs. [12 refs.]

Dermatoses associated with streptococci are common but the condition described in this paper does not appear to have found a place in the text books. It is a dry dermatitis, seen in Europeans as well as natives, but more often in the latter and in children in the authors' experience. The eruption may appear anywhere but is most common on the face. There is first an erythema which fades in a week or two when a scalliness is seen and depigmentation sets in, and in 2-3 months there is a depigmented patch, with ill-defined border (thus differing from the more marked and sharply defined areas of vitiligo) the affected areas are smooth or show a fine branny desquamation. Scrapings from the lesions were taken from seven patients. In two cases there was no growth though repeated attempts were made the condition had existed for 8 months in one and 12 months in the other and may have been receding. In the other five haemolytic streptococci were isolated (in one case together with a haemolytic *Staphylococcus aureus*) the duration of these positive cases ranged between 3 and 18 months. The best treatment is local rubbing in of a crude tar ointment pigmentation usually returns in about 3 months. That the condition is actually caused by the streptococcus is not proved but it is maintained that streptococci on the normal skin of persons in good health can never be considered as saprophytic. *H. Harold Scott*

BADHWAR, R. L., NAYAR, S. L. & CHOPRA, I. C. Indian Plants liable to produce Dermatitis. *Indian J. Agric. Sci.* 1945 June, v 15 Pt. 3 155-71 [16 refs.]

In India some 76 plants are known to produce irritation of the skin and even actual dermatitis in certain persons all are not equally susceptible. The

mode of action differs. Plants causing direct mechanical injury as by penetration of spines and thorns wounds from which may subsequently become infected and so set up dermatitis are excluded from this article. Included are —

(1) Those of the *Rhus* type and allied genera whose sap exudes when the plant is injured contact with the sap sets up a dermatitis due to a phenolic oily resin which it contains and which is known as toxicodendrol. It is not itself volatile but it may be conveyed in the soot of burning plants and also by insects which have alighted on an injured plant. Claim has been made that it is present in the pollen but say the authors this is not so. The irritation may be relieved by alkaline applications and a brief immunity can be produced by subcutaneous injection of an alcoholic extract but this immunity is very transient not lasting for more than a month.

(2) A second type of irritant is the *Urtica* type nettles are examples and the most potent of these in India is *Laportea granulata* the Fever nettle or Devil nettle. When the fragile hairs of the nettle penetrate the skin they break and the irritant in the hair enters the tissue. The protoplasm of the hairs is alkaline but encloses an acid cell sap which contains formic acetic butyric and other volatile fatty acids.

(3) A third group comprises plants which when ingested produce photosensitization and consequent dermatitis of unpigmented parts. Examples of this group are *Fagopyrum esculentum* and *Hypericum perforatum*.

Lastly there is (4) a miscellaneous group e.g. *Xanthium strumarium* which produces dermatitis in a few who happen to be sensitive to it the toxic principles are still undetermined. In others e.g. *Erigeron canadensis* there is an irritating essential oil. In *Podophyllum hexandrum* it is a resin in the root stock which is the irritant in other cases the mechanism is not known dust from dried plants may irritate the nasal and ocular mucosa.

The authors present in a table a list of the 76 plants known in India to cause dermatitis they give also the English and vernacular names their geographical distribution the part of the plant responsible for causing the dermatitis and where known, the toxic principle in each case. [A valuable piece of work]

H Harold Scott

MENDELSON H V Lemon Grass Oil a Primary Irritant and Sensitizing Agent. *Arch. Dermat. & Syph.* 1946 Feb v 53 No 2 94-8.

On the publication of his report of eight cases of dermatitis venenata due to lemon grass oil [see this *Bulletin* 1945 v 42 66] the author received samples of the oil from three sources one from Florida containing 75 per cent of citral an aldehyde constituent of the oil another from India also containing 75 per cent and a third from Guatemala with 76.2 per cent. He also received three samples of ionones in which the aldehyde is converted into a ketone. They are highly aromatic and are used in making perfumes and cosmetics.

The author made patch tests with all of these on 15 persons. All reacted with vesicles and bullae to the undiluted oils indicating a direct irritant action. dilution of the oil 1 in 10 or more, might result in a delayed reaction after 6 days indicative of induced sensitivity i.e. the diluted forms acted as sensitizers and when the patients were tested again 3 weeks later with the diluted oils erythema and vesiculation were observed on removal of the test patches after 48 hours application. In no instance was there any reaction to the ionones.

H Harold Scott

NÚÑEZ ANDRADE, R. Dermatitis causada por *Haematosiphon inodora* (Duges, 1892) [Dermatitis due to *H. inodora*] *Medicina*, Mexico 1946 Feb 10 v 26 No. 501 45-51 4 figs. English summary

"1 The author reports 21 cases in residents in Mexico City of a type of Dermatitis caused by bites of the chicken-bug called *Haematosiphon inodora* (Duges, 1892)

"2 One of the cases had been diagnosed as urticaria by food allergy another as *Prurigo mitis*, and the rest of them were considered as bites from bedbugs (*Cimex lectularius*)

"3 The dermatitis caused by the *Haematosiphon inodora*, was generally observed in all the inhabitants of the infected houses and furthermore almost all the houses in the same quarter were infested by the insects.

4 This dermatitis is polymorphous, having the appearance of hives [a popular name for urticaria and other skin diseases] papules vesicles venocapstules, scratches or scars

5 This dermatitis causes intense itching, burning sensations pain and sometimes general malaise and a rise of temperature derived from secondary infections."

PEANER, E. F. Coccioidomycosis at U.S.M.C. Air Station, Mohave, California. *U.S. Nav Med Bull.* 1946 Feb., v 46 No 2, 229-36

In view of the discovery of isolated cases of coccioidomycosis at a Naval Air Station at Mohave, California, an investigation was made into the possibility of the station being situated in an endemic area of the disease. All the staff were subjected to the coccioidin skin test as soon as possible after arrival at the station, and those on whom the result of the test was negative were tested again after an interval of about 4½ months. If the second test had a positive result it was assumed that infection had occurred in the interval between the tests. Twenty three men who were found negative by the first test gave positive reactions at the second test and none of these had been exposed to infection outside the station in the interval. In addition to these 23 seven men who were coccioidin negative on arrival at the station were admitted to hospital at some later time for an illness which was diagnosed as coccioidomycosis and all seven became sensitive to coccioidin during their illness. Clinical descriptions are given of these seven cases.

As none of the 30 men referred to had visited any known endemic focus of coccioidomycosis outside the station it was concluded that the infections must have occurred at the Mohave Air Station and that the vicinity of the station is an endemic area of coccioidomycosis.

J. T. Duncan

TWIDING, H. E., DIXON, H. M. & WEIDMAN, F. D. Penicillin in Treatment of Madura Foot. Report of Two Cases. *U.S. Nav Med Bull.* 1946 Mar., v 46 No 3 417-29 8 figs. [10 refs.]

The authors describe two cases of mycetoma—one caused by *Monosporium apiospermum* and the other by a newly-named fungus *Cephalosporium granulomatis* n.sp. Weidman and Kligman. In the first case the disease was of 7 years duration and some of the bones of the tarsus and metatarsus were involved. Penicillin treatment was instituted and this resulted in considerable improvement in the condition of the foot, although new lesions continued to appear. After a total dosage of 3,700,000 units, the patient was discharged with a prognosis of possible cure. Relapse occurred, however, and, after a further course of 2,100,000 units of penicillin had been given ineffectually the diseased foot

was amputated. In the second case the disease was of only two years duration and was limited to the soft tissues of the foot. Penicillin was given in doses of 20 000 units every three hours until a total of 2,300 000 units had been given. Improvement was rapid and apparently permanent and the patient was discharged from hospital six weeks after the conclusion of the penicillin treatment.

J T Duncan

## HEAT STROKE AND ALLIED CONDITIONS.

SHELLEY W B & HORVATH S M The Oral and Rectal Temperatures in Hot Environments. *Bull U.S. Army Med Dept* 1946 Apr v 5 No 4 459-61 1 fig

A comparison of rectal and oral temperatures of men working in a very hot room (120°F 36 per cent R H) environment showed the rectal temperature to range from 1.4°F below to 3.9°F above oral temperature averaging 1.2°F higher than the oral

LADELL W S S Changes in the Chloride Concentration of Sweat with Acclimatization. *Biochem J* 1945 v 39 No 5 xlviii-xlviii

The chloride concentration in serial sweat samples from the arms of subjects working in a hot humid environment rises as the exposure continues. Sweat is always hypotonic and the glands therefore must do work when they excrete sweat less work is done if the sweat is more concentrated, and the phenomenon reported may therefore be a manifestation of fatigue. Total salt loss is practically constant in a given individual from day to day for a given total of sweat lost so long as the rate of sweating remains the same. In rapid acclimatization there is no fall in sweat chloride concentration.

One subject lived in a hot room day and night and after the first few days the chloride concentration of his sweat no longer rose with time this was not due to salt lack. After the subject had left the hot room he lost this acclimatization effect. Other subjects who were exposed to heat for some hours every day over a period of many months showed the same effect but less markedly. Salt loss for heavy sweating became less showing diminished liability of the sweat glands to fatigue. This diminution in salt loss from sweat which occurs in hyper acclimatization should not be confused with the fall in chloride concentration in sweat which occurs as a result of deficiency of salt intake.

Charles Wilcocks

BURCH G E. & WINSOR, T Diffusion of Water through Dead Planar, Palmar and Tarsal Human Skin and through Toe Nails. *Arch Dermat & Syph* 1946 Jan v 53 No 1 39-41 3 figs.

LUCKTISH M TAYLOR A H COLE H. N & SOLLMANN T Protective Skin Coatings for the Prevention of Sunburn. *J Amer Med Ass* 1946 Jan. 5 v 130 No 1 1-6

This is an account of researches undertaken in December 1942 for the U.S. Army Air Force to provide an effective protective substance for the prophylaxis of sunburn. It was a collaboration between two physicists Lucktish and Taylor and two physicians Cole and Sollman. From previous observations on the ultra violet absorbing power of different substances it was decided

to concentrate only on preparations and mixtures containing any of the following: titanium dioxide, salicylates, zinc oxide, and petrolatum jelly. Various mixtures of two or more of these were tested, including several proprietary preparations. Several different varieties of petrolatum jelly without anything added were also tried. Physical tests showed almost complete absorption of ultra violet radiation by 0.03 mm. of a phenyl salicylate and petrolatum flavum mixture with or without added zinc oxide. Dark red vet. petrolatum was also selectively opaque to the erythema spectrum. Titanium dioxide was not so effective. For a biological test small areas of skin covered with the material being tested were exposed for varying periods to high intensity radiation and any development of erythema was noted without a protective coating on the skin. Erythema was usually produced with about 15 seconds exposure. It was found that zinc oxide diminished the protective power of the salicylate petrolatum mixtures, and that the dark red petrolatum gave complete protection for exposures of 20 minutes.

A factor of practical importance was resistance to washing, as the preparation was to be used by aviators who might be brought down into the sea. Poor resistance to washing eliminated preparations with a cold cream basis. Resistance to freezing was also necessary as the petrolatum would be carried in aircraft and might thus be frequently frozen. This eliminated mixtures containing water. The final recommendation was that two kits should be tried in practice and their respective values compared. Kit A of dark red vet. petrolatum and Kit B of dark red petrolatum with 10 per cent phenyl salicylate. The dark red petrolatum did not produce any irritation when applied daily to the skin of one investigator. [The effect upon sweating of the protective layer on the skin was not considered.]

W S S Ladd

## TROPICAL ULCER.

BRECHER G. Ambulatory Treatment of Tropical Ulcers. *Trans Roy Soc Trop Med & Hyg* 1946, Apr v 39 No 5 449-54. [10 refs.]

In the southern peninsula of the Republic of Haiti West Indies facilities for the treatment of ulcers of the leg in hospital were inadequate so a routine form of ambulatory treatment was adopted, with good results. Yaws is almost universal in that part of Haiti and skin lesions of yaws were present in nearly half the patients treated for ulcer of the leg, but the author concluded that most of the ulcers could be regarded as tropical ulcers.

The routine local treatment used was the one introduced for chronic ulcers of the leg by BAYVON of Bristol in 1799: heated adhesive strips [material not stated] 1 to 1 in wide were applied vertically or obliquely but not circularly and slightly overlapping each other so as to form an occlusive dressing over the ulcer and covering the surrounding skin for 3 ins above and below and 1 in. at the sides. This was covered by a bandage and the dressing was changed about once a week.

Systemic treatment was also given: neocarsphenamine was injected intravenously and bismuth subarsenate in oil intramuscularly, once a week on the same day.

Of 205 cases so treated 147 (71 per cent) were known to have healed, the other 58 having been lost sight of. Of these 147 cases 51 (35 per cent.) healed in under 30 days 74 (50 per cent.) in 30-60 days 10 (7 per cent.) in 60-90 days and 12 (8 per cent.) in 90-150 days. Of the 58 cases lost sight of, 46 had

improved and 12 were unimproved when last seen. Some complications are mentioned and there were two deaths which the author suspects were due to toxic nephritis caused by arsphenamine in patients with hookworm infestation. The author thinks that better results would have been obtained if the diet of the patients which was deficient in higher protein and calcium could have been improved.

J F Corson

## MISCELLANEOUS DISEASES

POWER, S  
572-3Funiculitis in British Troops in Ceylon. *Lancet* 1946 Apr 20

The author records an outbreak among the British troops of what for want of a better name may be called funiculitis. It occurred in Ceylon in 1943 after the onset of the south west monsoon. The disease was characterized by local induration of the spermatic cord due to thrombosis in the veins. Notes of two cases are given. No special treatment was required if seen at the onset the patients had a few days rest in bed, while if first seen later they were told to wear a suspensory bandage.

The author does not think that it was caused by filariasis although that would be suggested by its being endemic and seasonably epidemic in Ceylon. The locality was non-filarial none of the patients showed eosinophilia no filariae were found in the blood or hydrocele fluid, the pathology was not of the filarial type and filariasis is uncommon among Europeans [but see recent records of early filariasis among American troops abstracted in this *Bulletin*]. [Endemic funiculitis is stated by MANSON BAHR (Manson's Trop Dis. 1945 12th ed. London Cassell p 728) to be undoubtedly of filarial origin. *Ibid* 1909 v 1 227] and in Ceylon by CASTELLANI (*ibid* 1908 v 2, 15) who isolated a diplo-streptococcus which he thought was a secondary infection. CASTELLANI and CHALMERS (Manual of Trop Med. 1919 3rd ed. London Baillière Tindall and Cox p 1939) regarded it as a filarial condition with a superadded streptococcal infection. STEPHENS and YORKE (see The Practice of Medicine in the Tropics by BLAIR and ARCHIBALD 1923 v 3 1920) considered it to be due to filariasis. STITT also (Diagnosis Prevention and Treatment of Tropical Diseases 1942 p 1317) regards it as filarial in origin. It was reported from Kenya by JEWELL (this *Bulletin* 1925 v 22 890) who was convinced that the disease was *sui generis*. CASTELLANI (*ibid* 1918 v 11 212) saw a case in Macedonia.]

J F Corson.

## GENERAL PROTOZOOLOGY

SENEKJIE H A. & LEWIS Ruth A. An Inquiry Into the Growth Factor or Factors of certain Blood and Tissue Flagellates. *Amer J Trop Med* 1945 July v 25 No 4 345-8.

The authors have studied the culture requirements of species of *Leishmania* and *Trypanosoma cruzi* with a view to the discovery of the growth promoting factor which exists in the blood. It was found that the factor is present in serum but is not directly associated with albumin, euglobulin, pseudoglobulin or combinations of these. It is not present in haemoglobin nor in washed erythrocytes. It is destroyed at a temperature of 100°C. but partially survives

30 minutes exposure to 70°C. It was shown that para aminobenzoic acid, pyridoxine, nicotinic acid, thiamin and other vitamins tested, were all unable to take the place of the factor which is dialysable and is probably lost during the process of fractionating the serum proteins. C M Wesson

WEINMAN D. Human Toxoplasma. *Puerto Rico J. Pub. Health & Trop. Med.* 1944 Dec. v. 20 No. 2, 125-61 4 pls. [Refs. in footnotes.] [Spanish version 162-63.]

This is a useful general account of human toxoplasmosis based on published work of the author himself and others who have investigated the disease particularly in the United States during the past ten years. C M Wesson

DOW R. S. Toxoplasmic Encephalitis. Clinical Findings in 2 Patients from Pacific Northwest. *Northwest Med.* 1945 Dec. v. 44 382. [Summary taken from *J. Amer. Med. Ass.* 1946 Mar. 23 v. 130 No. 12, 821-2.]

Dow presents the histories of two patients with toxoplasmic encephalitis. The first was a child aged 2 who exhibited all the clinical manifestations of toxoplasmic encephalitis including (1) beaded or inactive chorio-retinitis (2) reduced vision, (3) strabismus, nystagmus and microphthalmos (4) intracerebral calcification (5) one convulsive seizure (6) internal hydrocephalus from a block at the aqueduct of Sylvius (7) retarded speech development and (8) mental deficiency. The case was complicated by the presence of a postoperative *Staphylococcus aureus* meningitis and wound infection. The serologic tests for toxoplasma had not been done and attempts to infect laboratory animals with spinal fluid were unsuccessful. The second patient, a girl aged 5 exhibited many of the signs and symptoms of toxoplasmic encephalitis. Treatment with sulapyridine was tried and continued for ten days maintaining a blood level of 5 to 10 mg. per cent. She seemed much improved for three weeks, but then seizures recurred. This observation and the results obtained in laboratory animals make it desirable to continue the use of sulfonamides whenever a diagnosis of toxoplasmic encephalitis is made and when there has not been extensive permanent cerebral damage. It is felt that the condition is more common than the reported cases would indicate and that a greater incidence will be found when knowledge of this disorder has become more generally available.

COWEN D & WOLF A. Toxoplasmosis in the Monkey. Acute Fatal Infection experimentally produced in a Young *Macaca mulatta*. *J. Infect. Dis.* 1945 Sept.-Oct. v. 77 No. 2, 144-57 11 figs. on 2 pls. [23 refs.]

Earlier attempts to infect monkeys with toxoplasma have given negative results as regards the demonstration of parasites by microscopic examination of tissues. Some evidence was obtained, however that rhesus monkeys as determined by inoculation of blood into mice or by serological tests might acquire a transient infection. In the experiments described in this paper attempts were made to infect by intracerebral and other methods of inoculation nine rhesus monkeys of which two were immature animals 7 months of age, two were young adults and three were pregnant females and two were infants the offspring of the pregnant animals. In addition a young African green monkey (*Cercopithecus aethiops*) and an adult baboon (*Papio doguera*) were also injected. Of these animals one young rhesus monkey succumbed to the infection and showed toxoplasmic focal myelitis and lesions in the rete testis. This is the first instance of active toxoplasmosis in a monkey with the production of lesions. Of the other 10 monkeys four gave a positive result

in serum neutralization tests for toxoplasmosis. Three monkeys including two of those giving a positive result in serum neutralization tests had myocardial lesions which were probably due to toxoplasmic infection though no parasites could be demonstrated in them. The attempt to produce congenital infection by the inoculation of the three pregnant monkeys was unsuccessful. From the experiments described in this paper which were carried out with a human strain maintained in mice and from the earlier work which is reviewed it is evident that primates are relatively unsusceptible to toxoplasmosis.

C M Wenyon

## GENERAL ENTOMOLOGY

CAMERON T W M. *Insecticides and Repellents in Modern Medicine*  
Reprinted from *McGill Med J* 1945 Oct. v 14 No 3 14 pp

This is a brief factual statement of information at present available on the insecticides and repellents now used in medicine and in it the author describes briefly the composition and effects of pyrethrum Lethane 384 Lethane 384 Special Thanite derris DDT DDD (the dichlorethane equivalent of DDT which has a similar action but is only about one-tenth as toxic to mammals) Gammexane the oils used as larvicides Paris green paradichlorbenzene orthodichlorbenzene and sodium arsenite. The repellents mentioned are oil of citronella with pyrethrum concentrate Indalone Rutgers 612 dimethyl and dibutyl phthalate a new repellent \MRI 201 developed in the United States and benryl benzoate.

In so short a paper the information given is necessarily compressed and the outline is brief. Nevertheless this is a useful summary which a student of tropical medicine could read with advantage. The author points out that medical entomology saw its modern beginning with the work of Manson and that it is now the backbone of public health work in the tropics. Information has accumulated so rapidly during the war that there is need of summaries of this kind to make the subject clear to those who wish to keep abreast of research but who are not actively engaged in it.

Charles H Wilcocks

DAVID W A L. *Factors Influencing the Interaction of Insecticidal Mists and Flying Insects. Part I—The Design of a Spray Testing Chamber and some of its Properties.* *Bull Entom Res* 1946 Feb v 36 Pt. 4 373-93  
4 figs [12 refs.]

The cabinet described was specifically designed for testing insecticides for use against mosquitoes but it can be used with other flying insects. It is a chamber in which temperature and humidity are controlled of 54.5 cu. ft. (1.543 litres) internal capacity into which the spray is atomized by an Aero-graph spray gun. The insects are exposed in wire frames covered with paper except for two wire mesh ends through which the spray can penetrate and knock-down counts can be made through special windows in the cabinet. These cages can be inserted or extracted without opening the cabinet door.

The author points out that the effects of variation in testing conditions are little understood, and testing of sprays has hitherto been done under arbitrary fixed conditions in order that tests may be repeated. Experiments were therefore planned to investigate various factors.

(i) The activity of the mosquitoes was very important because when the spray has evaporated down to floating particles (mist) the insecticide is mainly gathered by the insect as it flies through it. Very dilute pyrethrum preparations irritate the insects and stimulate flight, but this does not occur with DDT



sprays. The kill produced by the latter therefore depends to a large extent on the natural activity of the insects which varies in different cultures. To overcome this source of variability it is advisable to include a small, non-lethal concentration of pyrethrins so as to obtain uniform activity.

(ii) After the spray has been released, the more volatile fraction (kerosene) evaporates rapidly if the dose is below 15 cc. of liquid per 1 000 cu. ft. The chances of a drop of insecticide impinging on an insect are considerably reduced as the diameter falls below 5-10 microns. Therefore the concentration of non-volatile substance in the spray fluid is important and it can be shown that part of the effect of some synergizing materials (e.g. sesame oil, iso-butyl undecyleneamide) is due to the larger drops of spray left when they are present.

(iii) There is a positive correlation between temperature and susceptibility of the mosquito *Aedes aegypti* to pyrethrum as shown by results at 20°C. and 30°C.

(iv) The humidity during actual exposure however has little influence over normal ranges judging from results at 40 per cent. and 80 per cent. R.H.

(v) In this cabinet the time of introduction of the insects was investigated. Kill was highest when they were inserted before spraying and fell gradually to 10 minutes after spraying. The order of effectiveness of several formulae was not altered, however.

(vi) Some tests were made with insects flying freely in the cabinet, to compare with those in cages. The kills were higher in all cases when non-volatile constituents were added to the sprays but the relative results were similar.

J. R. BURTON

FAIRCHILD G. B. & BARREDA, E. A. DDT as a Larvicide against *Simulium*.  
*J. Econom. Entom.* 1945 Dec. v 38 No 6 694-6

The experiments aimed at eradication of *Simulium* spp. the vectors of *Onchocerca volvulus* in Guatemala and southern Mexico.

Experiments in Guatemala showed that addition of a 4 per cent. DDT emulsion concentrate to streams to give a dilution of one part DDT in ten million, killed *Simulium* larvae for a distance of ten kilometres along the stream.

Attempts to give a prolonged insecticidal action were made by compounding the DDT in blocks of plaster of paris in sawdust and in Esparto sponge guards. Effective kills resulted, but lasted only one or two days.

Further tests showed that DDT powder made into a suspension in water with a wetting agent gave kills as satisfactory as those obtained with emulsions. It seems possible that this is due to aqueous solution of DDT at a rate of one part in 10 to 15 millions of water.

J. R. BURTON

EBELING W. DDT Penetration prevented by adding Aluminum Stearate to DDT Kerosene Solutions. *J. Econom. Entom.* 1945 Dec. v 38 No 6 689-91 1 fig

The addition of 1 per cent. aluminum stearate to kerosene greatly retards its penetration into foliage leaves. The effect when a DDT solution in kerosene (4 per cent.) is used, is to keep the solution on the surface of the leaves so that DDT crystals are left exposed instead of penetrating the plant. The effect is sufficiently great for trees which have been sprayed with DDT solution plus aluminum stearate to be picked out from controls (DDT solution only) by the visible white deposit.

J. R. BURTON

HOCKING H. S. The Use of "666" in the Control of *Ornithodoros moubata* Murray East African Med J 1946 Feb v 23 No 2 50-55

As the tick *O. moubata* normally lives beneath the surface of the soil it is difficult to eradicate it from infested buildings. 666 (benzene hexachloride crude material containing 12 per cent of the active gamma isomer) and DDT were tested in the laboratory and the field against this tick. Although the laboratory tests suggested that the 666 sprayed at a rate of 1,250 mgm. per square foot should give complete control in native huts it proved less effective though it substantially reduced the tick population. A second application of 666 three weeks later seemed to eliminate the ticks. DDT also reduced the number of ticks but was considerably less effective than the 666  
Kenneth Mellanby

KEARNS C. W. INGLE L. & METCALF R. L. A New Chlorinated Hydrocarbon Insecticide J Econom Entom 1945 Dec v 38 No 6 661-8

The compound has the empirical formula  $C_{10}H_6Cl_6$  and is referred to as 1068. It is a colourless odourless viscous compound boiling at 175°C. It is readily soluble in most organic liquids and is completely miscible with odourless kerosene. The sample examined, which was at least 99 per cent pure showed no tendency to irritate skin or mucous membranes.

Insecticidal tests were made against a number of different insects in comparison with pure DDT and gamma benzene hexachloride. To the pea aphid (*Macrosiphum pisi*) the Colorado beetle (*Leptinotarsa decemlineata*) and the adult squash bug (*Anasa tristis*) 1068 was definitely more toxic than DDT.

As a residual film on wallboard 1068 was intermediate in speed of knockdown of *Anopheles quadrimaculatus* adults between DDT and benzene hexachloride the latter being most rapid. The order of efficiency as regards persistence was reversed DDT being most lasting.

Tests against larvae of *A. quadrimaculatus* indicated that the three substances were of the same order of toxicity.

Poot Grady tests with houseflies (*Musca domestica*) gave median lethal concentrations as follows: DDT 0.06 per cent and 1068 0.02 per cent.

Experiments in which solutions were delivered to the prothorax of individual roaches (*Periplaneta americana*) indicated a toxicity for 1068 three times as great as that of DDT.

Finally the various compounds were tested as stomach poisons for the grasshopper *Melanoplus differentialis*. The median lethal doses were —

gamma benzene hexachloride	5-10 micrograms per gram.
1068	12-25
DDT	over 50

J. R. Burvine

GRANETT P. & HAYNES H. L. Insect Repellent Properties of 2 Ethylhexanedol-1,3. J Econom Entom 1945 Dec. v 38 No 6 671-5

The compound 2-ethylhexanedol 1,3 has been known during the war as Insect Repellent No 612 the test number assigned to it at Rutgers University. It is a slightly viscous colourless liquid having a mild odour resembling that of witch hazel. It is stable under extremes of storage conditions and, unlike certain other repellents its solvent action on certain materials is relatively weak. It will not attack cellulose acetate cellulose nitrate polystyrene vinylite resin UYNS Lucite or Plaskon. The vapour pressure at 20°C. is only 0.01 mm. and it boils at 244 C. and freezes below -40 C. Solubility in water is 4.2 per cent. at 20 C.

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*J. Econom. Entom.* 1945 Dec. v 38 No. 6 604-9

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J. R. BUSTINE

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Fleas were not found on the pigs and they probably fed when the pigs were lying down.  
J F Corson

RADFORD C D. Notes on *Trombicula deliensis* Walch, 1923 (Acarina: Trombidulidae), with Description of the Adult. *Parasitology* 1946 Jan. v 37 Nos. 1/2 42-5 9 figs.

An account is given of experiments made in an attempt to rear *Trombicula deliensis* a mite whose larva is believed to be an important vector of scrub typhus (tsutsugamushi disease). It proved impossible to complete the whole life-cycle in the laboratory, but all stages were obtained: nymphs from larvae attached to wild rats, bandicoots and shrews obtained by trapping; and larvae from adults extracted from the soil. The nymphs died soon after moulting; too few larvae were obtained to continue the cycle. An account of the morphology of the adult which has not previously been described is given with some notes on its biology.  
Kenneth Mellanby

RADFORD C D. Larval and Nymphal Mites (Acarina: Trombidulidae) from Ceylon and the Maldive Islands. *Parasitology* 1946 Jan. v 37 Nos. 1/2 46-54 29 figs.

Some details of the morphology of the larvae and nymphs (together with the adult of *Neoschöngastia indica*) of several species of Trombiculid mites of possible medical importance are given with notes on the technique used when attempting to breed them in the laboratory. One new genus of Trombiculidae *Womeraleya* and the genotype, *W. minuta* is described: as this is parasitic on grasshoppers it is unlikely to be of medical importance.  
Kenneth Mellanby

CARTER H F & D ABRERA V St E. Mites (Acarina)—a probable Factor in the Aetiology of Spasmodic Bronchitis and Asthma associated with High Eosinophilia. *Trans Roy Soc. Trop Med & Hyg* 1946 Apr. v 39 No 5 373-87 1 chart. [23 refs.]

Twenty-five Ceylonese patients all with a high eosinophilia (over 3 000 per cmm. as against a normal 500 per cmm. for individuals in the tropics) and all but one with bronchial asthma or other respiratory symptoms were investigated. Treatment was given with organic arsenicals and 24 out of 25 responded satisfactorily both as regards clinical symptoms and as to eosinophilia the latter being greatly reduced within three weeks.

Samples of sputum from these patients were collected with rigorous precautions to prevent contamination. Mites mostly tarsonemids or tyroglyphids were recovered from all cases. After treatment with arsenicals the number of mites was strikingly reduced. There is no doubt that these mites came from the lungs.

Most of the mites collected are normally found among food and stored products and it is suggested that some of these may be able at times to colonize the bronchi. Cases are described in which allied mites have been recovered from human tissues. These creatures are almost ubiquitous in tropical countries and can live under very diverse conditions so it is not impossible that they can invade living tissues. In some of the cases described it seems

In tests in which 1 cc. of material was applied to 100 square inches of skin the compound compared with dimethyl phthalate as follows —

Insect	Time to first bite	
	612	Dimethyl phthalate
<i>Aedes aegypti</i>	9 hr	7-8 hr
<i>Anopheles quadrimaculatus</i>	1 "	2 "
<i>Aedes sollicitans</i>	6 "	4 "
<i>A. cantator</i>	3-4	1½-2
<i>Anopheles albimanus</i>	8 "	1 "
<i>A. punctulatus foveolatus</i>	1½-2 "	1 "
<i>Stomoxys calcitrans</i>	8 "	3½
<i>Simulium</i> spp.	4 "	4 "
<i>Phlebotomus</i> spp.	2 "	4 "
<i>Chenopthalides canis</i>	on treated suits	
<i>C. felis</i>		
<i>Exorombiula</i> spp.	30± days	30± days
<i>Acariscus maroni</i>		

It will be seen that "612" compares well with dimethyl phthalate, being more effective against all insects except *Anopheles quadrimaculatus* and the fleas.  
J R Burrina.

HATOFF A. Desensitization to Insect Bites. *J Amer Med Ass* 1946 Mar 30 v 130 No 13 850-54

"In a series of 129 susceptible infants and children 4 out of 5 were benefited by the use of flea antigen. This constitutes a demonstration of one method of developing host immunity to insect bites. The importance of this demonstration lies in the possibility of the use of such a method as an adjunct in the control of insect borne diseases."

FREEMAN R. B. The Pig as a Host of *Pulex irritans* L. (Siphonaptera, Pulicidae)  
Reprinted from *Entomologist's Monthly Magazine* 1946 Jan. 30 v 82 19-21 [10 refs]

The human flea, *Pulex irritans* is found on many mammals but most of them especially rodents are probably not true hosts the flea being unable to maintain permanent colonies on them some however are true hosts the domestic pig being probably the most important while the dog is also often infested [see MACARTHUR this *Bulletin* 1946 v 43. 602]. The author gives references to reports of the infestation of pigs in Great Britain, the United States of America, Argentina, Australia, and Morocco this *Bulletin* 1923 v 23 916]. LEWIS (Ga. Leckford Estate Andover 1936 v 1 104) reported an outbreak on a farm which had been famous for Geas for the past thirty years or more "they became a serious pest after the arrival of pigs on the farm."

A severe infestation of the pigs on a pig farm at Adderbury, Oxfordshire was investigated in 1938 all the farm buildings the two cottages and the yards were heavily infested and the surrounding fields contained considerable populations of the fleas "wherever the harmless looking mass of bits of straw and dry loam was disturbed it was seen to be a seething mass of jumping fleas" [quoted by the author from a report. Since the pigs were removed (apparently in 1940) severe outbreaks of flea infestation were noted twice in 1942 and once

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Kenneth McIlanby

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probable that the mites were really established as parasites in the lungs in others the mites were probably casual invaders.

The relation between the mites and the symptoms is discussed. A patient sensitized to the mites and their products would be likely to show more acute symptoms with only a few mites in the lungs than an unsensitized individual with a great parasite population. This may account for some apparent discrepancies in the results. The thesis that the mites may be the cause of the asthmatic symptoms and the eosinophilia seems to be well established by this work. [See also the previous paper on the subject, this *Bulletin* 1945 v 42, 73]

Kenneth Mellanby

## LABORATORY PROCEDURES

BROWN R. L. Comparative Studies on Enteric Protozoal Parasite Ova and Cysts Concentrating Procedures. *Amer J Trop Med* 1945 July v 25 No 4 375-8

The author has made a comparison of two techniques for the concentration of protozoal cysts and helminth eggs in faeces. These were the de Rivas acetic-acid-ether method (this *Bulletin* 1928 v 25 447) and the zinc sulphate method. In all cases the methods were applied to an emulsion of the faeces in physiological saline filtered through two layers of gauze. In the de Rivas method 5 cc. of the filtrate were shaken up with 30 cc. of 5 per cent acetic acid. The mixture was filtered through gauze, and an equal volume of ether was added. This was shaken until it jellied. It was then centrifuged. Two drops of the deposit were taken up and examined for cysts or ova. In the zinc sulphate method 5 cc. of the filtrate were diluted with 60 cc. of tap water and centrifuged. The fluid was poured off and the deposit taken up with tap water and again centrifuged. This process was repeated till the supernatant fluid remained clear. The sediment was then taken up in zinc sulphate solution of specific gravity 1.180 and again centrifuged. Two drops of the surface film were then pipetted off for examination. It was found that generally the zinc sulphate technique proved to be the more reliable though it occupied more time than the de Rivas method which in the case of some cysts and ova failed to concentrate at all. Furthermore the de Rivas method produced more distortion. For routine examinations the zinc sulphate method is to be preferred as it was much less selective concentrating more nearly uniformly all cysts and ova with a minimum of distortion.

C. M. Henson.

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

NAPIER, L. E. Teaching of Tropical Medicine. *Trans Roy Soc Trop Med & Hyg* 1946 Feb v 39 No. 4 273-82 Discussion pp. 283-300  
[MANSON BAHR, P. GORDON R. M. MACDONALD G. HODGE E. H. V. DREW W. R. M. STANFIS H. S. TROWELL, H. C. CHRISTOPHERS R. NAPIER, L. E. (in reply) SHORTT H. E.]

Dr Napier began his address by stating that Great Britain was rapidly losing any lead which it may have had in the field of tropical medicine and that the subject appeared to have been relegated to the place of a specialisation about which the general practitioner need know nothing and with which the ordinary undergraduate student should not be burdened. This unfortunate attitude was exemplified in the *Goodenough Report* where the existence of

parasites other than bacteria was apparently not recognized and in which there was no suggestion that the undergraduate student need be introduced to diseases which were not prevalent in his own country moreover under the heading of postgraduate teaching clinical tropical medicine was dismissed as a subject that could not possibly be taught in Britain The speaker emphasized the fallacy of segregating so-called tropical medicine of teaching parasitology to the student with bacteria as the only examples of parasites and while in his later years of teaching him virtually nothing of the pathology symptomatology and therapeutics of tropical diseases

Dr Napier next discussed how this unfortunate state of affairs might best be remedied In the undergraduate years it was of importance to avoid further overloading of the curriculum but much might be done by introducing the student during his pre-medical years to the pathogenic micro-organisms and worms and by substituting both in name and scope parasitology for bacteriology If this system were adopted it would leave the pathology symptomatology and therapeutics of important tropical diseases (many of which presented excellent opportunities for the teaching of the general principles of preventive medicine) to be taught in the systematic lectures on medicine in the wards and out patient departments when the occasion arose Such teaching would necessitate a generous supply of material for the practical classes in parasitology and for the teaching of clinical pathology and histology clinical material would have to be made available for the later years In the United States this difficulty was faced and overcome very early in the war by the co-operation of the Army Medical School at Washington which distributed suitable material to all the medical schools in the country Later some of the schools through their tropical connexions contributed to the common pool and the organization is at present receiving an abundance of material from the thousands of postgraduate students now serving in various tropical fields The importance of clinical material is obvious and a considerable amount of such material is now available in Britain although it is sometimes missed Dr Napier considered that during the next few years there would be an increasing number of cases of tropical diseases among the personnel of the fighting forces and among civilians whom the war has taken into the tropics Even in the absence of such cases however much could be done with the aid of a good set of lantern slides preferably in colour or better still with cinema films

As regards postgraduate teaching Dr Napier thought that it would be a tragedy with considerable political and financial as well as medical repercussions if we were to allow America or any other country to take the lead in the postgraduate teaching of tropical medicine and to attract to their country doctors and even patients from India and the Dominions the Colonies and foreign countries who would otherwise have come to London or Liverpool In London there was an abundance of clinical material which would show a marked increase during the succeeding years but at present no hospital where it could be collected The most crying need to-day was a tropical medical centre where all such persons returning from the tropics could go for diagnosis and treatment There was a popular misconception that in medical practice in any tropical country one would encounter a very large variety of the diseases usually labelled tropical Actually there were few if any places in the world where one could see a better selection of tropical diseases than in London The object of a post-graduate course in tropical medicine should be not to make the student an expert in all tropical diseases but to give him additional knowledge to enable him to take advantage of the opportunities to become an expert which would be provided in his subsequent practical experience in whatever tropical centres he might visit The speaker seriously questioned the value of instituting a higher diploma of specialist status in tropical medicine



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Volume I is devoted to a consideration of the intestinal protozoa, leishmaniasis, trypanosomiasis and spirochaetosis, including rat-bite fever, syphilis and yaws, etc. Under these headings dealt with from the South American point of view a vast amount of information is given, somewhat uncritically most of it being quotations from the literature.

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C M Wrayson.

# TROPICAL DISEASES BULLETIN

Vol. 43]

1946

[No. 8.

## CONTROL OF SCHISTOSOMIASIS

By J J C BUCKLEY D.Sc.

*Lecturer in the Department of Parasitology London School of Hygiene and Tropical Medicine (University of London)*

Any approach to the problem of schistosomiasis control whether it be an investigation or some more direct attempt to reduce the incidence of the disease will naturally be made from the standpoint of one or both of the main principles—prevention and treatment. Preventive methods in schistosomiasis are concerned with some phase in the rather complicated but well known life-cycle of the parasite and their efficacy and expediency are determined by factors which may vary with local exigencies of topography and custom. Treatment in schistosomiasis which in this instance obviously implies mass treatment involves the use of drugs experience has shown that certain derivatives of antimony are the only effective if not highly efficient curative agents

### *Prevention*

In recent years a considerable amount of research has been carried out and field trials have been attempted in several regions to control schistosomiasis by the preventive method with varying degrees of success. A general account of these is presented here under three headings 1 Protection of snail-bearing waters from fouling and infection. 2. Destruction or reduction of snail populations. 3 Avoidance of cercarial infection.

1 *Protection of snail habitats from infection*—The means for achieving this very desirable objective and thus breaking the bilharzia life-cycle at its outset may not always be to hand nor easily applied, but the advantages of this form of control are manifold whether it be achieved by education and propaganda or by some more directly practical measures. Considerable success in this direction appears to have attended the efforts of the Sudan Medical Service [Report of the Sudan Medical Service for the year 1936 (this *Bulletin* 1938 v 35 266)] Sanitary measures were employed, which comprised the placing of all villages at least 300 metres from snail infested canals which in addition were fenced and the provision of good wells and latrines near the villages. These measures, combined with treatment have resulted in substantial reductions in the schistosomiasis incidence in parts of the Northern Province in the Wadi Halfa District and in the Blue Nile Province

2 *Destruction of snails*.—The most obvious and usually the most practicable method of breaking the bilharzia life-cycle is to kill or get rid of the snail intermediaries and since the researches and recommendations of LEIPER in Egypt (this *Bulletin* 1915 v 6 437) opened up this field of attack in 1915

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most of the anti-bilharzia campaigns in subsequent years have been based on this principle.

The methods of snail control in operation or suggested in endemic areas are mainly as follows: the introduction of chemical or organic poisons into snail habitats; the removal of snails by manual labour; the removal of vegetation and other necessary elements in their environment; biological control by the introduction or encouragement of natural enemies or unsuitable types of vegetation; the reconstruction of natural watercourses (e.g. by canalization, cementing or covering); flushing, draining and drying of watercourses and the removal of unnecessary bodies of water.

The most widely-used chemicals for snail destruction are copper sulphate, copper carbonate, slaked lime and ammonium sulphate. KHALIL and AZIM [this *Bulletin* 1938 v 35 667] used copper sulphate in a concentration of 5 parts per million for 5 days in the streams and channels of the Dakhla Oasis, Egypt, and found it effective. BAUGÉ [this *Bulletin* 1942, v 39 768] also obtained good results in Southern Tunisia with copper sulphate in a focus of *S. haematobium*. This salt has the disadvantage of rendering water unfit for human consumption for a while, but in Southern Rhodesia MOZLEY [this *Bulletin* 1942, v 39 11] found that malachite (mineralized basic copper carbonate) is just as effective and less toxic; on the other hand it is more expensive and less soluble. The system of control employed in Fayoum Province [BARLOW and AZIM, this *Bulletin* 1943 v 42, 1017] combines copper sulphate treatment of the larger canals with manual clearance of snails and vegetation from the lesser water-courses. The concentration of copper sulphate varies from 15 to 50 parts per million according to the amount of silt and vegetation present. At Oran in Algeria, a new focus of urinary schistosomiasis appeared after the initiation of an irrigation system, which created an immense habitat favourable for snails (ALCAY MARILL and MUÑOZ this *Bulletin* 1943 v 40 467). It was suggested that these canals be controlled by emptying and cleaning, but it is pointed out that it would be a measure of only temporary value since the canals become restocked with snails from some natural source which should be found and controlled. [The dangers of "man-made" snail habitats of another kind have been indicated by MOZLEY (this *Bulletin* 1945 v 42 516) in Southern Rhodesia, where small artificial pools polluted with human dejecta and litter become more heavily stocked with snails than are natural waters.]

In Venezuela, LUTTERMOSER [this *Bulletin* 1943 v 40 849] records the successful control of *Planorbis (Australorbis) glabratus* vector of *S. mansoni* by the application of recently slaked lime to the waterways. He found that a 0.1 per cent. solution kills snails and eggs in a day or less. In field practice several treatments of canals, cement tanks and  $\frac{1}{2}$  kilometre of a river kept the water free of snails for 6 months but one treatment every 3 months was usually sufficient. Lime has the advantage also of being non-toxic to domestic animals and cultivated land, and possesses a useful anti-bacterial and cercarial action. JANKEN [this *Bulletin* 1945 v 42, 1018] also tested the effect of slaked lime in Catende, Pernambuco against *Planorbis (A.) centrisetatus* and obtained 100 per cent. snail mortality with a strength of 4-5 parts per thousand after 24 hours. The use of lime is deprecated by MOZLEY [this *Bulletin*, 1945 v 42, 518] in Southern Rhodesia since by increasing the lime availability it may encourage snail development in lime-deficient areas. He considers that quicklime is ineffective against bilharzia snails as a result of his experience in treating a small stream containing *Physopsis* and *Blomphalaria*.

Doubts about the efficacy of drying as a means of snail control have been raised by several workers. BAUMPT [this *Bulletin* 1942, v 39 868] states that *Planorbis (A.) glabratus* has considerable resistance to drying, and that after

nate drying and filling of canals every 15 days is not effective. In laboratory experiments this species survived 50 days of drying more severe than would occur in nature. According to BARLOW and AZIM [this *Bulletin* 1945 v 42 1017] *Bulinus truncatus* is not killed by emptying and drying canals for 40 days and in laboratory tests this species revived after 12 months and *Planorbis boissyi* after 10 months desiccation in mud.

The amphibious intermediary of *S. japonicum* *Blanfordia* (*Oncomelania*) *nosophora* requires a somewhat different method of attack. MRYAJIMA [this *Bulletin* 1939 v 36 623] describes the control of this species which lives partly in the water of ditches and partly on their muddy and weedy margins by applications of quicklime to the water in a strength of 1 per cent. for 10 hours while snails outside the water are killed by a steam jet. Control measures against *S. japonicum* must take into account the fact that it is harboured by other definitive hosts as well as man. WU [this *Bulletin* 1941 v 38 43] found the following animals naturally infected in China: sheep goats house-rats dogs cats oxen buffaloes and horses.

Biological control of snails by means of natural enemies such as ducks hedgehogs and fish is undoubtedly valuable but is practicable in only a limited range of circumstances. A case for hitherto control by fish in South Africa and Rhodesia has been stated by CAWSTON [this *Bulletin* 1937 v 34 797]. Biological control by means of aquatic plants such as *Pistia stratiotes* has been suggested by MOZLEY [this *Bulletin* 1940 v 37 483] who noted that in Zanzibar and Tanganyika Territory snails are scanty in water whose surface is completely covered by aquatic or semi-aquatic plants. Biological control by planting *Balanites* trees along snail-infested watercourses has also been suggested. ARCHIBALD [this *Bulletin* 1934 v 31 114] found that the fruit of this tree (*B. aegyptiaca* in Tropical Africa Arabia, Egypt and Palestine) if treated in a certain way produces a poison which is highly fatal to snails and WAGER [this *Bulletin* 1936 v 33 557] noted that the fruit of the South African species *B. maughamsi* has similar properties. It is also very toxic to other forms of aquatic life such as tadpoles frogs fish etc. and its value as a snail-killer may therefore be offset by the danger of upsetting the balance of life in natural waters.

3 *Avoidance of cercarial infection*—Individual prophylaxis is theoretically simple and consists merely in avoiding skin-contact with or the drinking of infected water but this doctrine implies that persons liable to exposure are aware of the life-cycle of the parasite and may be nullified by the requirements of agricultural practice in some countries. BRACKETT [this *Bulletin* 1940 v 37 149] showed experimentally that the cercariae responsible for schistosome dermatitis penetrate skin mainly when water is evaporating from it so that vigorous wiping after bathing is a useful prophylaxis. The well known fact that schistosome cercariae do not live longer than 48 hours in water can also be used in prophylaxis in certain circumstances.

Researches on cercaricidal substances have mostly centred about the effects of chlorine. WITENBERG and YOFFE [this *Bulletin* 1938 v 35 600] found chloramine more efficient than gaseous chlorine or sodium hypochlorite the concentrations necessary being 0.22 part per million residual after 10 minutes application for chloramine 0.42 for sodium hypochlorite and 0.6 for gaseous chlorine. MAGATH's experiments [this *Bulletin* 1943 v 40 156] indicated that chlorination of 0.2 part per million [residual of 0.1 p.p.m. after 30 minutes] kills cercariae of *S. mansoni* in 30 minutes. OLIVER GONZÁLEZ BIAGGI and RIVERA LEÓN [this *Bulletin* 1946 v 43 347] suggest from experimental results that a minimum exposure of 20 minutes to the effects of a chlorine solution yielding a minimum chlorine residual of 0.5 part per million may be sufficient to render cercariae non-infective. KRAKOWER [this *Bulletin* 1941 v 38 376]



subjected the cercariae of *S. mansoni* to a variety of physical conditions and found that their normal span of life in rain water is 24-48 hours rarely 72 hours. They survive up to 14 days at 5°-6°C. but remain motionless, while freezing is rapidly fatal. Above 34°C. the mortality increases and at 45°C. all die in 30 minutes. Strong electric light induces activity and shortens the span of life while ultraviolet light and direct sunlight are both fatal, but the heat of the sun may also be an adverse factor in this instance. Extremes of pH outside the 4.6-10 range are fatal and cercariae are rapidly killed in a 1.5 per cent. solution of sodium chloride.

#### Treatment.

The efficacy of prevention in an anti-bilharzial scheme must necessarily be greatly enhanced by concurrent treatment of the infected population, which stems the source of snail-infection at its origin but the prolonged and tedious procedure of present-day methods of chemotherapy in schistosomiasis is very unsuitable for mass treatment. In this connexion the researches of ALVES [this *Bulletin* 1945 v 42, 815] and ALVES and BLAIR [*ibid* 1946 v 43 344] on an intensive treatment with sodium antimonyl tartrate in Southern Rhodesia are most opportune and have an important bearing on the present problem. These authors devised a course of treatment of only 2 days duration which consists of six intravenous injections each of 1-2 grains of S.A.T. In a trial of 100 cases all positive by intradermal tests and by examination of stools or of urine none was passing eggs two months after treatment and a high proportion were negative by the skin test. Toxic complications were unimportant and transient. This treatment was subsequently modified to a course of one day only with smaller dosage [ALVES below p. 752] which was tried out on a group of 131 cases all positive by the skin test. Four weeks later none of these was passing eggs. While the follow up of these cases is as yet incomplete and the possibility of relapses is admitted the importance of the treatment is manifest, for it provides a means of rapidly disinfecting an infected population for a time at least, which would offer a breathing-space in the struggle to break the life-cycle in bilharzias since our snail-killing will be at a peak at, and immediately after the time when the population's infectivity is at its lowest and those adult snails which escape killing will also escape infection.

If the promise held out by these researches is fulfilled a great advance in the control of schistosomiasis will have been achieved.

## SUMMARY OF RECENT ABSTRACTS \*

### VII. HELMINTHIASIS

#### General

VASILKOVA (p. 569) has examined the water of the river Moskva, in Russia, for helminth eggs. The main source of contamination was the effluent from a sewage works, and in water from this source 4,500 eggs per cubic metre were found, including those of *Ascaris Trichuris Taenia* and *Diphyllobotrium*. *Enterobius* and *Dicrocoelium* eggs were found in the river water. Some of the eggs were viable. A degree of natural cleansing of the river water takes place by settlement, but better methods of purifying sewage water are needed. In the meantime people may infect themselves from the river.

The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945 v 42. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

NISO (p 473) discusses appendicitis in which there is associated helminth infestation of the appendix. He found worms in 3.17 per cent of 1763 appendices examined. In by far the majority of cases the worm was *Enterobius vermicularis*.

OLIVER-GONZÁLEZ and TORREGROSA (p 45) have isolated a substance from certain helminths infesting man which is related to human isoagglutinins.

A Symposium on Anthelmintics (p 570) has been published in the United States.

ROGERS (p 299) has made a very thorough study of the anthelmintic activity of hexylresorcinol and tetrachlorethylene using the perfused small intestine of rats infested with *Nippostrongylus muris* for the purpose. Details of the many observations should be sought in the original abstract but the main conclusions are that the efficiency of hexylresorcinol is reduced by sodium taurocholate, and that the drug is adsorbed on to mucin which prevents its penetration into the parasites. The latter appear to stimulate the formation of mucus in the intestine and are to a very considerable extent protected by the mucus on the intestinal wall. Tetrachlorethylene on the other hand stimulates *N. muris* to leave mucus and to enter fluids in the intestinal lumen. It is not inhibited by bile salts and acts rapidly in the rat. Sodium laurate and sodium oleate show intrinsic anthelmintic properties: the former activates hexylresorcinol more than the latter.

PARANJAPÉ *et al* (p 571) have investigated the anthelmintic action of certain synthetic lactones and compounds allied to santonin. In their work they used earthworms, commenting on this fact LAPAGE gives reasons why *Ascaris* of the pig would provide a more satisfactory test.

### *Trematodes*

*General*—SILVEIRA (p 46) in a discussion of pulmonary schistosomiasis notes that this condition is much less common in *S. mansoni* than in *S. haematobium* infections and explains this by reference to routes available in the venous system to each of these trematodes. Nevertheless pulmonary schistosomiasis due to *S. mansoni* is not uncommon. There are two stages: acute (during the stage of migration through the lung) which is the toxæmic form and may even be fatal; and chronic (due to adult worms or eggs in the lung). Clinically there are two forms with respiratory symptoms or with symptoms of embarrassment of the pulmonary circulation. The only certain diagnosis is the finding of eggs in the sputum, since radiological signs are not characteristic.

*Schistosoma haematobium*—Vesical schistosomiasis is prevalent in Angola. In one area SARMENTO (p 1015) found infection in 60 per cent of children and in 21.5 per cent of adults. ANDREASEN and SURI (p 742) report what appears to be the first recorded case of infection with *Schistosoma haematobium* contracted in India. [The importance of such a finding is sufficiently obvious: the disease was well established in this patient and the authors think that he probably acquired it in his home village.]

GORSSE and ACCART (p 395) review the results of treatment of over 200 cases of urinary schistosomiasis. They argue that the best estimate of treatment can be obtained by cystoscopy and they describe the appearances to be seen by this means at different stages of the infection. The results of treatment with tartar emetic, Fousdim and anthiomaline were not satisfactory: the last of these being the best. Nevertheless antimony though not specific, is the most useful drug but in some cases seems to be insufficient by itself. An intensive course of treatment of schistosomiasis with a preparation of sodium antimonyl tartrate is described by ALVES (p 815). The whole course

consists of a total dosage of 12 mgm. of the drug per kgm. body weight and the injections are given intravenously at intervals of 2 to 2½ hours over a period of 30 hours with a break of some 16 hours after the first day of treatment. The injections are given very slowly and the drug is well diluted in glucose-saline. Results appear to be promising.

STEPHENSON (p. 572) has treated nine patients infested with *Schistosoma haematobium* with stilbamidine, but concludes that the action of this drug is too uncertain to justify its routine use in urinary schistosomiasis.

*S. mansoni*.—In Pernambuco infection with *S. mansoni* is common, and MAGALHÃES (A.) *et al.* (p. 1016) show that the infection rate is highest in late childhood and young adult life. Males are rather more commonly affected than females.

DI GIACOMO and MAYER (p. 47) make the point that infection with *S. mansoni* may be very insidious, and that stool examination should be made on all persons from endemic areas whether or not there are suggestive symptoms.

WRIGHT and ROBERTS (p. 215) describe the early symptoms of infection with *S. mansoni* in a boy who shortly after contracting this infection showed creeping eruption which the authors think was due to larvae of *S. mansoni*. At the time when the creeping eruption was noticed, the boy was suffering from urticaria. He subsequently developed intense eosinophilia.

BERCOVITZ *et al.* (pp. 47-572) found small ulcers on proctoscopic examination of recruits in Porto Rico who had eggs of *S. mansoni* in their faeces. The blood picture showed little departure from the normal.

ALMY and HARPER (p. 646) report a case of chronic infection with *S. mansoni* in which Banti's syndrome developed. ALMY and HARPER (p. 815) also describe a case of long-standing infection with *S. mansoni* in which there were associated signs of Banti's disease.

SAXENIA (p. 393) describes two patients, with bilharzial myocarditis in whom the Stokes-Adams syndrome was present. MEIRA and RAMOS (p. 572) discuss two forms of myocarditis which may occur in infestation with *S. mansoni* but in part of a thesis on *S. mansoni* infection MAGALHÃES (B. F.) and DIAS (p. 1016) make a note of the fact that in 22 autopsies they failed to find myocardial lesions, and that ova have not been found in the heart muscle. They think, therefore that it is highly improbable that there is a cardiac form of the disease.

CRAM *et al.* (p. 646) have shown that the snail *Tropicoorbis kayanensis*, indigenous to the United States is susceptible to infection with *S. mansoni*.

*Bulinus truncatus* is a carrier of bilharzia in the Fayoum Province of Egypt. BARLOW and ABDEL AZIM (p. 1017) describe control measures used in Egypt against this and other snails. There are two main methods—mechanical clearance of small streams by means of standardized hand nets, and the use of copper sulphate in larger canals. For the latter concentrations of 15-50 parts per million are required in field work. Snails live a long time, but probably not more than 2 years—desiccation for 40 days cannot be relied upon to kill them since they have been known to revive after 12 months desiccation in mud. JAWSON (p. 1018) has found that slaked lime in a strength of 4-5 parts per 1,000 and copper sulphate in a strength of 2 parts per 1,000 are effective in killing *Australorbis centronatus* the host of *S. mansoni* in Pernambuco.

KRAKOWER *et al.* (p. 133) have found that eggs of *S. mansoni* in guineapigs kept on a diet deficient in vitamin C, tend to show disintegration of the shells. Deficiency of vitamin C did not, however interfere with the development of *Schistosoma*.

*S. japonicum*.—An account of the symptoms of the early stage of schistosomiasis japonica is given by THOMAS and GAGE (p 1018). There is usually fever with headache cough possibly abdominal symptoms and in some cases urticaria. The liver is usually enlarged and tender the spleen less commonly so. Eosinophilia is characteristic. Eggs are found in the faeces some 6–10 weeks after infection they may be present in patients who have had no more than trivial symptoms.

In the *Bulletin of the U.S. Army Medical Department* (p. 1019) the treatment of schistosomiasis japonica is discussed and Fouadin and tartar emetic are the drugs advocated. Each may be toxic, and each should be injected slowly. Fouadin should be tried first. For details of administration the original abstract should be consulted.

*Other trematodes*.—STEPHENSON (p 474) has found that *Fasciola hepatica* will live for 60 hours at 38°C in a solution containing NaCl KCl CaCl<sub>2</sub>, borax and glucose of pH 8.6. This is adequate for the preliminary testing of anthelmintics in such tests carbon tetrachloride was found to be innocuous though it is probably the best anthelmintic in man.

WITENBERG (p 396) has found a fluke, *Clinostoma complanatum* in man it caused laryngo-pharyngitis. This infection is apparently due to the eating of fish infested with metacercariae of the fluke.

CORT (p 905) discusses the germ-cell cycle in the digenetic trematodes. The subject is complex, and cannot briefly be dealt with the original should be consulted by those interested.

### Cestodes

In a series of four papers TÖTTERMAN (p 215) discusses the anaemias which occur in a small proportion of people infested with *Diphyllobothrium latum*. He estimates that about 14 per cent of people in Finland are infested by this worm. The well-known anaemia is indistinguishable from pernicious anaemia, but there is another and more common form, a light hyperchromic anaemia, which he regards not as a stage in the development of the former but as a separate condition. In this anaemia liver preparations have no effect but improvement follows administration of a vermifuge, whereas in the pernicious form liver is useful. The light anaemia is probably due to absorption of toxins from the worm which alone will not cause the 'pernicious' form.

Treatment of the pernicious anaemia with yeast, which is rich in Castle's extrinsic factor has given good results but the author has not been successful with certain extracts of hog stomach. He argues that the pernicious anaemia of *D. latum* infestation occurs in patients who have become sensitized to the tapeworm and quotes his own experiments which showed that in sensitized persons but not in normal controls administration by injection of an alcoholic extract of the worm tended to produce a 'pernicious' form of anaemia.

GIBSON (p 396) reports the discovery of species of *Diphyllobothrium* in trout in England, and UKSWORTH (p 397) discusses the recent findings of tapeworms of this genus in fish and in birds in England and Ireland. He concludes that the evidence is against their being *D. latum* but in comment LAPAGE suggests that the relationship between the tapeworms of birds and *D. latum* needs further study. BAYLIS (p 906) also discusses the species of *Diphyllobothrium* found in trout and in birds in the British Isles and differentiates them from *D. latum*.

DIXON and HARGREAVES (p 907) report on 284 cases of cerebral cysticercosis. In 89 per cent of proved cases radiographic examination of the skull failed to show the parasites and the point is made that only in a minority of cases do the degenerative changes in these intracerebral cysts go on to calcification.

The authors discuss prognosis, and in comment MACARTHUR points out that relapse may follow a symptom-free period lasting as long as 20 years. The original paper should be read by those interested in this condition.

ARANA and ASEJO (p. 908) have made ventriculographic examinations in 20 cases of cerebral cysticercosis in which the parasites were sub-tentorial. All cases were verified. The radiological findings should be studied in the original.

SELMAN (p. 816) describes a case of eosinophilia of the blood and of the cerebrospinal fluid, in a patient who showed signs of meningeal irritation. The author thinks that this was probably a case of cerebral cysticercosis. A similar case is referred to by APFELBAUM and WEXBERG (p. 816).

MAZZOTTI (p. 647) gives information on cysticercosis in Mexico and again refers to the high proportion of positive results obtained in infestations with *T. saginata* by examination of the perianal region by means of swabs. This suggests the possibility of auto-infection, and similar findings have been made in the case of *T. solium* but not, apparently, to anything like the same extent, probably because the proglottides of *T. solium* do not emerge spontaneously as do those of *T. saginata* but only with the faeces.

The same author (pp. 134-393) made 108 examinations of the perianal region, by means of the Graham adhesive cellulose tape method, in 10 persons infested with *Taenia saginata*. Of these examinations, 85 per cent. were positive, whereas with direct smear examination of faeces, the proportion was very much smaller. Eggs were also found on other areas of skin between the neck and the knees, and on the underclothes. On examining the proglottides of the worm he found that the branches of the uterus communicate with the exterior when the proglottid is detached, and that disintegration is therefore not essential for expulsion of eggs.

NISO (p. 909) thinks that Acramil, an acridine derivative of the mepacrine type, is the ideal anthelmintic for the treatment of infestation with *Taenia saginata*. Of 41 patients 34 were cured by a single treatment, and four others after more than one. Details of administration are given in the original abstract.

RIVAS *et al.* (p. 910) give details of the statistics of hydatid disease in patients treated at the Institute of Clinical Surgery, Buenos Aires. The amount of information given cannot satisfactorily be summarized, and the original abstract should therefore be consulted.

BARKITT and THOMAS (p. 474) have written a long paper on pulmonary hydatid disease. It is not possible to do justice to all the points raised, for which the original should be consulted but certain statements may be noted. The presenting symptom is usually haemoptysis, but the first signs and symptoms may be due to anaphylaxis. Sudden expectoration of a large amount of clear salt tasting fluid is diagnostic of the rupture of a simple cyst. Pulmonary hydatid cysts should never be aspirated. The parasite should be removed at the earliest possible moment—the safest way to enucleate a simple cyst is to treat it as a lung abscess, but in a selected group of cases the treatment of choice is lobectomy.

CASTRO (p. 573) discusses hydatid disease of bone. Prognosis in these cases is grave and for affected bones of the limbs, amputation is usually necessary. Hydatid disease of the spine is always fatal. HOWORTH (p. 817) also refers to the fact that treatment of hydatid cysts of bone is still unsatisfactory.

Treatment of infestations with *Hymenolepis* in children by means of male fern given in cycles was found unsatisfactory by PODYAPOLSKAYA and ISACHENKO (p. 573) who therefore experimented with other drugs given in association with male fern. Of these the most effective was methylene blue,

but yatren was also useful. For details of administration the original abstract should be consulted. GORIACHEVA (p 575) has tried this method and regards it as the best yet available. He prefers it to the use of pumpkin seeds or of full doses of male fern both of which he tested.

In a study of the vitamin requirements of cestodes ADDIS and CHANDLER (p 302) found that *Hymenolepis diminuta* was markedly affected by lack of vitamins in the diet of the host, if the latter was a female rat but not if it was a male (Chandler). They therefore worked with female rats and discovered that the vitamin concerned was riboflavin. If this was withheld, the number and size of the infesting cestodes were smaller than in rats on full diet and the longer the vitamin had been withheld the more marked the effect. On the other hand when vitamins A, D, E and B were lacking the worms grew rather longer than shorter. The cestodes obtain their protein by absorption direct from the mucosa of the host not from the contents of the intestine [and presumably they obtain riboflavin in the same way].

KOURI (p 477) reports that up to 1944 more than 70 cases of infestation with *Inermicapsifer cubensis* had been reported usually in young children. Man is probably not the normal host and appears to be an unfavourable host but examination of a large number of mammals, arcan insects and crustacea has failed to reveal the parasite.

Charles W. Wilcocks

[To be continued]

## MALARIA.

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The author records the results of observations made by an expedition organized by the Moscow and Uzbek Malaria Institutes for the study of the causes of a serious outbreak of malaria in the province of Samarkand (Middle Asia) and to devise measures for its control. A detailed analysis is given of the epidemiological situation in the Urgut district which represented the focus of the epidemic. This area is characterized by a high endemicity of malaria of all the three types the malignant tertian form being predominant. There are two efficient vectors *A. maculipennis sacharovi* and *A. superpictus* and abundant breeding places in the form of rice-fields, swamps and a network of canals. By the time the expeditions arrived and were in a position to undertake the necessary anti-malarial measures fully 100 per cent of the local population (about 40 000) had had malaria, and a high proportion among them were carriers. With the view to dealing with the existing situation and to preventing an epidemic in 1943 the following measures were adopted —

(1) Systematic anti-relapse treatment with acriquine (=mepacrine) (0.3 gm. daily in single dose) to which in the last cycle plasmocide (=pamaquim) was added. (2) chemoprophylaxis of the entire population with acriquine + plasmocide (0.3 gm. acriquine + 0.04 plasmocide on two successive days followed by an interval of 5 days). (3) early detection of all acute cases of malaria and parasite-carriers and their systematic drug treatment. (4) monthly examination of the population for the detection of carriers and for observation of the indices.

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Charles Wilcocks

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These measures against the parasite in the human host were combined with anti-mosquito measures, including improvements affecting mosquito breeding places.

In undertaking all these measures the investigators realized that methods which were capable of eliminating malaria from localities with a low incidence of malaria were insufficient to cope with the infection in a highly affected focus. Nevertheless, the expeditions have succeeded in their main task—to prevent a fresh epidemic outbreak. The anti-malarial campaign resulted in a lowering of the incidence of malaria, in an absence of severe forms (coma, etc.) without fatal cases, as well as in raising the labour output of the population.

C A Hoare

YAGUJINSKAYA, L. V. [Malaria Vectors in the Northern Part of the Urgut District, after the Observations of 1943.] *Med. Parasit. & Parasitic Dis.* Moscow 1945 v 14 No. 3, 47-58 8 figs. [In Russian.]

This paper is devoted to the results of a study of the anopheline population in the Urgut District of the Samarkand Province (Middle Asia) in which a severe outbreak of malaria occurred in 1942 (see ПРОКОПЕНКО above). A detailed description is given of the bionomics of the mosquitoes, of which the most common are *A. bifurcatus*, *A. maculipennis sacharovi* and *A. superpictus* while *A. algeriensis* and *A. pulcherrimus* occurred only singly. *A. hyrcanus* has never been found in dwellings. In view of the predominance of *A. maculipennis sacharovi* as compared with the other species during the epidemic season and on account of its known epidemiological peculiarities, this mosquito is regarded as the most important local vector of malaria. This conclusion is fully supported by the oocyst and sporozoite rates revealed by dissection.

C A Hoare

FLOCK, H. & ABOWNING, E. Sur *A. darlingi* Root 1928 en Guyane française. Gîtes larvaires, morphologie et moeurs. [*A. darlingi* in French Guiana Breeding Places, Morphology and Habits.] *Publ. Inst. Pasteur Guyane Cayenne*. 1943 No. 65 7 pp [11 refs.] Sur le rôle de *A. darlingi* Root 1928 dans la transmission du paludisme en Guyane française. [The Role of *A. darlingi* in Malaria Transmission in French Guiana.] *Ibid* No. 71 10 pp. [Summary taken from *Rev. Applied Entom.* Ser. B. 1946 Apr., v 34 Pt. 4 57-8.]

In the first paper data on the breeding places of *Anopheles darlingi* Root, and the house-frequenting habits of the adults are reviewed from the literature and from observations in French Guiana, where it was first recorded in 1934. Adults and larvae have since been found along the whole length of the island of Cayenne and at various places in the interior but not in the town of Cayenne which is swept by Atlantic winds. The breeding places differ greatly but are usually in open situations sheltered from wind and sometimes partly shaded from the sun. The water is acid in reaction and of low mineral content and the vegetation varied. A study of eggs laid by females from different localities in French Guiana showed that there were forms corresponding to those described by Root and by Galvão, Lane and Corrêa and an intermediate form. Sometimes they occurred alone and sometimes all three together in one batch. The adults reared from these eggs showed no differences of any consequence and the authors conclude that *A. darlingi* cannot at present be divided into varieties. *A. darlingi* represented 91 per cent. of the *Anopheles* taken in houses throughout the year but only 12 per cent. of those taken in woods.

In the second paper it is pointed out that it is most abundant in June-August when malarial endemicity is increasing and that it prefers to feed on man although it has been observed to attack fowls and ducks and is occasionally taken in traps containing horses. Data are given from the literature on its natural infection with malaria parasites in other countries. Dissection of 542 females taken in French Guiana showed seven to be infected, six with oöcysts and two with sporozoites. As the mosquitos were not from large centres of population *A. darlingi* is thought to be an important local vector in spite of this comparatively low infection rate. Of females that survived for more than four days after being fed on gametocyte carriers five out of 14 became infected with *Plasmodium falciparum* the commonest malaria parasite in French Guiana, and one out of six with *P. vivax*. In one instance infection with *P. falciparum* developed to the sporozoite stage.

FLOCH H & ABONNENC E. Sur *A. aquasalis* Curry 1932. *Publ. Inst. Pasteur Guyane* Cayenne 1943 No 68 9 pp 2 figs. *A. aquasalis* Curry 1932 et paludisme en Guyane française. Infection naturelle et infection expérimentale [Experimental and Natural Infection of *A. aquasalis* in French Guiana.] *Ibid* No 72 8 pp. [Summary taken from *Rev. Applied Entom.* Ser. B 1946 Apr v 34 Pt 4 58-9]

The species of *Anopheles* of the subseries *oswaldi* known to occur in French Guiana when these papers were written were *A. sinuatus* Senevet & Abonnenc, and *A. oswaldi* Peryassó both of which had been found only in the interior and *A. aquasalis* Curry (previously referred to as *A. tarsimaculatus* Goeldi). In view of the discovery in Venezuela of the three closely related coastal species *A. nuñez-torres* Gabaldon, *A. rangeli* Gabaldon, Cova-García & López and *A. goeldii* Rozeboom & Gabaldon, data on the wing and tarsal colouring of these three and *A. oswaldi* and *A. aquasalis* are quoted from Gabaldon & Aguilera. However they do not make accurate differentiation possible and in order to identify with certainty the mosquitos occurring on the coast of French Guiana and referable from examination of females to *A. aquasalis* progeny were reared from several caught in nature. Examination of the adults and male hypopygia showed them to agree with *A. aquasalis*. There was considerable variation among eggs of a single batch. This is the only species of *Anopheles* occurring in houses in Cayenne but over the rest of the coast it represents 51 per cent. of the *Anopheles* taken in woods but only 6 per cent. of those taken in houses. It attacks both man and animals. Larvae were found at all seasons and occurred in fresh and brackish water. They were very adaptable surviving transfer from salt water (19 gm. sodium chloride per litre) to fresh and from fresh to salt.

Further information is given in the second paper on the occurrence of *A. aquasalis* in Cayenne, where it is found on outside walls and in dark corners of kitchens, ground floor rooms and sheds and rarely in mosquito nets. Dissection of 117 females from various parts of the colony failed to reveal any natural infection with malaria parasites. However undoubted cases of locally acquired malaria occurred in 1940 in Cayenne where there is no other *Anopheles* and experimental infection was obtained with *Plasmodium falciparum* in seven out of 30 females that survived for more than four days and with *P. vivax* in ten out of 28. In one case infection with *P. falciparum* developed to the sporozoite stage. *A. aquasalis* thus appears to be more susceptible to *P. vivax* than *A. darlingi* Root [cf. preceding abstract], but it is thought to be only a secondary vector of malaria in view of its habit of feeding indifferently on man or animals.

FLOCH H & DE LAJUDIE P Sur les divers indices endémiques du paludisme en Guyane française. [Endemic Indices of Malaria in French Guiana.] *Publ Inst Pasteur Guyane* Cayenne. 1945 No 107 10 pp. [11 refs.] [Summary taken from *Rev Applied Entom.* Ser B. 1946 Apr v 34 Pt. 4 60]

The results of recent malaria surveys made in the interior of French Guiana are given and compared with similar data for Cayenne. The spleen, parasite, and gametocyte rates were 44, 24 and 7 in the interior and 12, 6 and 0.3 in Cayenne. *Plasmodium falciparum* was responsible for 85 per cent. of cases whereas 68 per cent. were attributable to *P. vivax* in 1917. A list is given of the 21 species of Anophelines known to occur in French Guiana. All have been recorded in earlier papers of this series except an unidentified species of the subgenus *Stethomyia* of *Anopheles*. *A. darlingi* Root is stated to be the principal vector of malaria, though it has not yet been taken in the regions dealt with in this survey. *A. aquasalis* Curry and *A. triannulatus* Neiva & Pinto (*bachmanni* Petrocchi) have been experimentally infected but attempts to infect *A. pessoni* Galvão & Lane, and *A. mediopunctatus* Theo failed.

MUSPRATT J On *Coelomomyces* Fungi causing High Mortality of *Anopheles gambiae* Larvae in Rhodesia. *Ann. Trop. Med. & Parasit.* 1946 Apr., v 40 No. 1 10-17 2 figs. on 1 pl.

The finding of fungal parasites of the genus *Coelomomyces* in larvae of *Anopheles gambiae* at Livingstone, Northern Rhodesia, in March 1941 led the author to make further observations, until May 1945.

He was able to distinguish four types of the parasite. Type *a* was the commonest and was also the most important, for in nature it killed large numbers of larvae of *A. gambiae*. It was seen occasionally in larvae of *A. squamosus* and *A. rufipes* and once in *A. rivulorum* but it seems unlikely that the fungus seriously affects larvae of the *funestus* series. Larvae of *A. pretoriensis* became infected when transferred to an infected pool. Larvae of *A. costalis* and *A. rhodesiensis* taken from water containing infected larvae of *A. gambiae* showed no sign of fungus, and no culicine larvae (except a few *Culex simpsoni*) were infected. Laboratory-bred larvae have not yet been successfully infected.

Type *b* is rarer than type *a* and has been observed in larvae of *A. gambiae* and *A. squamosus*. Type *c* was found only in larvae of *Aedes scutophagoides*, and type *d* in the stem of a sedge (*Cyperus* sp.) but not in any mosquito larva or any other aquatic insect.

The fungus seems to be associated with the heavy, dark-brown, loamy clay locally known as mopane clay. Most of the infected pools are exposed to sunlight. Infected larvae are found only during three or four months in the wet season, that is, from December onwards, and the mortality of *A. gambiae* larvae in observed pools in that period is estimated to be often as high as 85 per cent.

The author describes the appearance of the infection in the larvae and the process of germination. He is convinced that the matter is worthy of a more thorough investigation, particularly as regards the possibility of using the fungus in the biological control of *Anopheles gambiae*. H. S. Leeson

RABONI C. Alcuni sintomi respiratori nell'infezione malarica primitiva. [Respiratory Symptoms in Primary Malaria.] *Riv Patol e Clin d Tubercolosi* 1944 May-June v 18 Nos 5/6 96-104 [11 refs.]

STOVHAM F V Traumatic Rupture of Large Spleens. *Indian Med. Gaz.* 1945, Nov v 80 No 11 547-11 3 figs. (1 on pl)

Malaria is by far the commonest cause of enlargement of the spleen in Asiatics in India. Rupture may be spontaneous or caused by trivial violence though more usually it is due to traffic accidents or brawls and is associated with other injuries. In the majority of cases shock and haemorrhage are so severe that the patient quickly succumbs so that probably only one in every 20 of such patients reaches hospital alive but spontaneous arrest of haemorrhage by clotting sometimes occurs even after severe damage. Delayed haemorrhage from the injured spleen is usually due to such a clot giving way. The malarial spleen unlike that in acholuric jaundice or splenic anaemia is seldom adherent to surrounding tissues. Kala azar produces large soft fragile spleens which later become firm and fibrous these may be ruptured by violence or by tearing of the capsule when spleen puncture is done. Enteric fever tumours and blood disorders are not important aetiological factors in traumatic rupture of the spleen in Asiatics.

The patient with ruptured spleen is profoundly shocked with local signs of trauma, and possibly haematuria from coincident damage to the left kidney. The abdomen becomes distended, but true rigidity is usually absent. The pulse is rapid and of poor volume, and the blood pressure is low. X ray examination which should not be done if the diagnosis can be made without it, may show raising of the left cupola of the diaphragm. Fixed dullness in the left flank with shifting dullness in the right flank (Ballance's sign) is unreliable as it depends on the size of the spleen and the amount and site of the blood clot. Liver dullness may be diminished. There is usually little or no recovery from the initial shock and the condition deteriorates progressively unless operation is undertaken promptly. A high operative mortality must be accepted if lives are to be saved and delay is justified only when the patient's condition is so low that immediate operation would be fatal or in cases where the injury occurred more than 12 hours previously and the patient's condition is stationary. The author does not think that time should be spent in resuscitation and transfusion, as these may cause further bleeding and add to the shock.

Cyclopropane is the anaesthetic of choice though chloroform with free administration of oxygen was used in the majority of the author's cases in Persia Iraq and India. Continuous pentothal administration was used in some of his later cases. A continuous intravenous infusion of saline, or of blood if available, is started at the commencement of the operation. A long mid-line incision is recommended, to which a transverse incision may be added if more room is required. As blood tends to remain fluid when shed into the peritoneal cavity the peritoneum is opened by a small incision and as much as possible of the fluid blood is sucked out by a Higginson's syringe to be added to the transfusion fluid after straining. The peritoneum is then opened widely the clots are removed and the operation completed in the usual manner. A sudden worsening of the patient's condition often occurs as the spleen is dislocated. Drainage is not employed unless there has been injury to the tail of the pancreas. Post-operative transfusion is continued till the systolic blood pressure is 100 mm. but failure to recover from shock is often seen. Simultaneous rupture of the left kidney can in most cases, be treated on conservative lines. A left pleural effusion of moderate amount is of no significance but associated injury to the chest is likely to cause trouble.

W. L. Harnett.

FLOCH, H. & DE LAJUDIZ, P. Sur les divers indices endémiques du paludisme en Guyane française [Endemic Indices of Malaria in French Guiana.] *Publ. Inst. Pasteur Guyane Cayenne*. 1945 No 107 10 pp. [11 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1946, Apr., v 34 Pt. 4 60.]

The results of recent malaria surveys made in the interior of French Guiana are given and compared with similar data for Cayenne. The spleen, parasite, and gametocyte rates were 44, 24 and 7 in the interior and 12, 6 and 0.3 in Cayenne. *Plasmodium falciparum* was responsible for 85 per cent. of cases, whereas 68 per cent. were attributable to *P. vivax* in 1917. A list is given of the 21 species of *Anopheles* known to occur in French Guiana. All have been recorded in earlier papers of this series except an unidentified species of the subgenus *Stethomyia* of *Anopheles*. *A. darlingi* Root is stated to be the principal vector of malaria, though it has not yet been taken in the regions dealt with in this survey. *A. aquasalis* Curry and *A. triannulatus* Neiva & Pinto (*beckmanni* Petrocchi) have been experimentally infected but attempts to infect *A. pereslei* Galvão & Lane, and *A. mediopunctatus* Theo failed.

MUSPRATT, J. On *Coccomomyces* Fungi causing High Mortality of *Anopheles gambiae* Larvae in Rhodesia. *Ann. Trop. Med. & Parasit.* 1946 Apr. v 40 No. 1 10-17 2 figs. on 1 pl.

The finding of fungal parasites of the genus *Coccomomyces* in larvae of *Anopheles gambiae* at Livingstone, Northern Rhodesia, in March 1941 led the author to make further observations, until May 1945.

He was able to distinguish four types of the parasite. Type *a* was the commonest and was also the most important for in nature it killed large numbers of larvae of *A. gambiae*. It was seen occasionally in larvae of *A. squamosus* and *A. rufipes* and once in *A. rivulorum* but it seems unlikely that the fungus seriously affects larvae of the *funestus* series. Larvae of *A. pretoriensis* became infected when transferred to an infected pool. Larvae of *A. costanti* and *A. rhodesiensis* taken from water containing infected larvae of *A. gambiae* showed no sign of fungus, and no culcine larvae (except a few *Culex simpsoni*) were infected. Laboratory-bred larvae have not yet been successfully infected.

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ABONI C. Alcuni sintomi respiratori nell'infezione malarica primitiva. [Respiratory Symptoms in Primary Malaria.] *Riv Patol e Clin e Tubercolosi* 1944 May-June v 18 Nos 5/6 96-104 [11 refs]

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W. L. Harnett.

C

KYKER, G. C. CORMACKER, W. E. & McEWEN Mildred M. The Ultraviolet Irradiation of Quinine. *J Biol Chem.* 1946 Feb v 162 No 2, 353-61 2 figs. [16 refs.]

It is known that solutions of the cinchona alkaloids exposed to light of short wave-length undergo some change whose nature has not been definitely established. In the present investigation the photodecomposition of quinine and quinidine has been studied following irradiation with sunlight or an ultra violet lamp. The antimalarial activity of the irradiation products will be reported on at a later date. Solutions of pure material containing 5 mgm. quinine per ml. were exposed to sunlight in very dilute sodium hydroxide (mixed with alcohol to retain the base in solution) in water and in different strengths of hydrochloric acid in Pyrex as well as in soft glass containers. Control samples were kept in the dark. Estimations of the amount of quinine still present were made at intervals up to 275 days in each series by three different methods. In the first two methods the turbidimetric procedure of KYKER WEBB & ANDREWS (*J Biol Chem.* 1941 v 139 551) was employed with and without previous ether extraction of base, respectively. By the third method specific optical rotation was determined. In the irradiation experiments with ultraviolet light, quartz cells which freely transmitted the wave-lengths of light absorbed by the alkaloid, served as containers. Solutions of quinine dihydrochloride and sulphate and quinidine sulphate were used for exposure. Turbidimetric and fluorimetric methods of analysis were employed. The results of irradiation with u.v. light were qualitatively similar to those obtained by exposure to sunlight but the former method was more effective in causing photodecomposition and there was only slight discoloration of the solutions. The results of analysis by the different methods did not give very concordant results. It appeared, however, that the amount of decomposition depended on the pH of the solution on the concentration of alkaloid present and on the optical properties of the containers but not on the nature of the alkaloidal salt. Control tubes kept in the dark showed no discoloration or alteration in quinine content. No evidence of the chemical nature of the changes occurring was obtained. J. D. Fulton

BISHAY A. Quinine Amblyopia. *Brit. J Ophthalm* 1946, May v 30 No 5, 281-7 4 perimeter charts

SHIERS D. Cerebral Excitement following Mepacrine Therapy [Memoranda.] *Brit. Med. J.* 1946 May 16 782-3.

On three separate occasions in 1945 a soldier felt and showed signs of great mental exuberance and other emotional disturbance after taking mepacrine. There was no personal or family history of mental instability and the Wassermann reaction of his blood was negative. The symptoms are well described in the present report, which relates to the third occasion, after his admission to the Royal Masonic Hospital in December 1945 for an attack of benign tertian malaria.

He was given mepacrine 0.7 gm. daily for 2 days then 0.6 gm. daily for 7 days. Almost immediately he was seized with a feeling of extreme exhilaration and well-being. He began almost to burst with energy running instead of walking, and doing everything at top speed. His mind became choked with ideas which occurred at all times of the day and night. While many of these never reached maturity some of them resulted in the patient writing poems and creating new designs for houses and buildings. At times, too, he was seized with an uncontrollable desire to cry and as a result would weep copiously although inside he felt, so he said, extremely happy.

The first occasion was in February 1945 in Assam, when he took suppressive doses of mepacrine 0.1 gm. daily with similar effects the second was in August 1945 when he had his first true attack of malaria and took mepacrine 0.2 gm. t.d.s. for 5 days in addition to quinine, and, later pamaquin again the same effects were produced during the taking of mepacrine.

He slowly recovered from this third attack on ceasing to take mepacrine and receiving phenobarbitone. [For other references to mental effects due to mepacrine (atebrin) see this *Bulletin* 1937 v 34 151 159 1938 v 35 516 1939 v 38 872 1941 v 38 337 1945 v 42, 9 253 629 784 The author refers also to ALLEN *J Med Ass Georgia* 1937 v 26 62.]

J F Corson

KINO E. J GILCHRIST M & TARNOKY A. L. Excretion Products of Mepacrine a Spectrophotometric Study *Biochem J* 1946 v 40 No 1 Proc. Biochem. Soc. 111

SPINKS A. TOTTEY Mary M & MAZGRAITH B G The Pharmacology of Paludrine and some other New Antimalarials. *Biochem J* 1946 v 40 No 1 Proc. Biochem. Soc. 1

SPINKS A. & TOTTEY Mary M Studies on Synthetic Antimalarial Drugs. XV Hydrolytic Determination of Paludrine. *Ann Trop Med & Parasit* 1946 Apr v 40 No 1 101-12 7 diagrams

The method employed by the authors for the estimation of Paludrine [this *Bulletin* 1946 v 43 400] now in use for one year has been slightly modified and the time required for hydrolysis has been greatly reduced. Special precautions such as the need for clean apparatus and purity of reagents as well as points in technique are fully described. Briefly the method consists in basifying the material containing the drug with NaOH followed by extraction with a benzene-ethanol mixture. The base is taken up in N/4 hydrochloric acid and hydrolysed to *p*-chloroaniline at 20-25 lb pressure for 3-4 hours. The latter substance is then diazotized and coupled to form an azo dye and matched against a standard in a photoelectric or visual colorimeter within an hour of preparation. The procedures used with different materials such as plasma, blood urine faeces bile or tissues vary slightly in detail for these the original should be consulted. With plasma and blood the method can be used for concentrations down to 50  $\mu$ gm. per litre. With lower concentrations a modified coupling method is employed in conjunction with a Spekker absorptiometer and the sensitivity is increased 3-5 times.

A special investigation was made regarding the best conditions of hydrolysis for Paludrine and closely related compounds to *p*-chloroaniline these are embodied in the above method. It was found that Paludrine can be sufficiently hydrolysed even at 100°C. to allow of estimation if an autoclave is not available. N- $\beta$ -sulphatoethyl-*m*-toluidine was found to be a more satisfactory coupling agent than  $\beta$ -1-naphthylethylenediamine. Using the former reagent the authors investigated the stability of the dye solution. The value for the extinction coefficient at the wave-length of maximal absorption was unaltered after 17 hours but there was at that time an increased absorption at lower wave-lengths. Hence the recommendation to examine the dye solutions within one hour after development of colour if a spectrophotometer is not available. Isolation of Paludrine from the urine of human subjects receiving the drug showed that the amount recovered was in fair agreement with that obtained by the hydrolytic method of estimation, and indicates that it is a suitable procedure.

J D Fulton



The result of these improvements is shown in the morbidity statistics. In 1943 the highest weekly peak of malaria incidence was equivalent to an annual rate of 410 cases per thousand. In 1944 the corresponding peak rate was 151 per thousand, and in 1945 up to the end of June it was 36 per thousand.

The paper has several illustrative examples including a detailed account of an outbreak in a Division which failed to take adequate precautions when it detrained at a very highly malarious station. The final illustration of the standard reached shows that the malaria casualties in a Corps at the highly malarious station of Venexia-Giulla were no more than those in a Corps in a non-malarious station in Austria.

[The author has an interesting story which is very much to the credit of some individuals and organizations very much to the discredit of others. It does not seem to the reviewer to set out the relevant facts adequately or in a sufficiently dispassionate manner for the reader to form an independent opinion on controversial subjects.]

G Macdonald

KNOWLES F L & SMITH C. S. DDT Residual House Spray—a Method of Malaria Control in Rural Areas. *Pub Health Rep* Wash. 1945 Oct. 28 v 60 No. 43 1274-9

As a test of the practicability of mosquito control by the use of DDT an area of 36 square miles containing 545 houses occupied by plantation negroes on a low standard of living was chosen and 513 houses were treated with DDT the remainder being left as controls. Power-driven spray apparatus was used, and the stock solution consisted of DDT 23 per cent xylol 71 per cent and Triton X 100 6 per cent diluted with water to give emulsions of final strength of 5 2½ and 1 per cent DDT. The 5 per cent emulsion gave an actual dose of 64 mgm. per square foot, and presumably the other two doses of 32 and 12 mgm. per square foot.

The full cost of the work is not stated. Material and labour costs for each house amounted to 74 cents, while transport overhead and other charges had to be added to this, but the total cost per house was probably less than one dollar.

Efficiency of the insecticide was judged by counts of the numbers of *Anopheles quadrimaculatus* in treated and untreated houses. Spraying was completed by August 14 and the percentage reduction in treated houses was —

	5 per cent. DDT	2½ per cent. DDT	1 per cent. DDT
August 15 to September 15	97	85	63
September 15 to October 14	88	74	68
August 15 to October 14	94	81	66

G Macdonald.

See also the papers by SIMMONS and his colleagues on the use of DDT in mosquito control (below p. 789)

GIULIO C. L'eradicatione della malaria in Italia (The Eradication of Malaria in Italy) *Riv di Malariologia* 1946 Feb v 23 No 1 31-5 English summary (3 lines)

BISHOP Ann & GILCHRIST Barbara M. Experiments upon the Feeding of *Aedes aegypti* through Animal Membranes with a view to applying this Method to the Chemotherapy of Malaria. *Parasitology* 1946 Jan. v 37 No. 1/2 83-100 2 figs. [25 refs.]

This paper records the results obtained from a continuation of the investigation previously reported by these authors [this *Bulletin* 1945 v 41

731] the object of which was to obtain sporozoites free from all trace of glandular tissues in order to test the action of drugs directly upon them. It can be seen from the summary of their paper quoted below that the authors have succeeded in this object and the technique they describe should be of considerable value in obtaining viable sporozoites free from glandular tissue. Later in the paper the authors state "A complete knowledge of the mode of action of any antimalarial drug which had been proved to eradicate sporozoite-induced infections in experimental animals would involve a study of its action upon sporozoites *in vitro* and upon the primary tissue phase in culture. By such *in vitro* methods it would be possible to compare the action of a drug upon the sporozoites and primary tissue phase of the species of malaria used in the experimental animal (e.g. *Plasmodium gallinaceum* in chicks) with its action upon the sporozoites and primary tissue phase of any of the species of *Plasmodium* of man. In order to approach such a study it is essential that a method should be devised whereby sporozoites can be obtained free from gland tissue and bacterial contaminants. The method in general use whereby sporozoites are obtained for injection is by dissecting out the infected glands from the mosquito and teasing them apart or grinding them up. Such a method is laborious and though suitable for infection experiments is unsuitable for the study either of the direct action of drugs upon sporozoites or for tissue culture for it is impossible to ensure that all the sporozoites are free from traces of tissue and bacterial contaminants may be present. [With this statement the reviewer is in complete agreement but, whereas the technique described by Bishop and Gilchrist is admirably adapted to fulfil the first requirement *viz.*, freedom from gland tissue it does not appear to solve the second problem that of obtaining sporozoites free from bacterial contaminants since the feeding mosquito not being sterile, will presumably introduce them when piercing the membrane with its proboscis.]

During the course of their investigation of the ejection of sporozoites by *Aedes* in the act of feeding, the authors made a series of other interesting observations which add considerably to our knowledge not only of the optimum temperature at which the food should be offered but also as regards how its nature and manner of presentation determine whether it is passed directly into the stomach or first into the diverticula.

The authors summarize their findings as follows —

1 Membranes prepared from chicken skin provide a suitable medium through which *Aedes aegypti* females may be induced to gorge.

2. Under suitable conditions the proportion of female *A. aegypti* which will gorge through membranes though more variable than when a living chick is offered is great enough for experimental purposes.

"3 It is shown that the gorging reaction in *A. aegypti* is provoked by a heat gradient between the environment and the food limiting membrane.

4 The feeding reactions of *A. aegypti* towards whole blood fractions of blood and other substances have been studied. It was found that (a) whole blood and red corpuscles in saline *when ingested through membranes* go directly into the stomach which becomes fully distended (b) haemoglobin in plasma or distilled water is ingested to a lesser degree than whole blood or red corpuscles in saline and plasma alone is rarely ingested but all these pass to the stomach (c) sweet solutions containing glucose or honey are seldom imbibed through membranes and pass to the stomach or diverticula, but only the diverticula are fully distended.

"When offered as *open drops* (a) blood is seldom ingested but if ingested passes to the stomach (b) haemoglobin in plasma or water or plasma alone are very rarely ingested but pass mainly to the stomach (c) sweet solutions

infected with *P. velinum* the drug being given subcutaneously. All but one compound of each series showed activity. The most active was 2238F with a chemotherapeutic index of 1/50. Its toxicity was low and the authors believe that it merits clinical trial.

J. D. Fulton.

ZAIN H. Malariaimmunität und Rezidiventstehung unter Berücksichtigung der Endothelstudien (*Plasmodium gallinaceum*). II Mitteilung [Immunity and Relapse in regard to the Endothelial Stages of *P. gallinaceum*] *Dtsch Tropenmed Ztschr* 1944 Apr-May v 48 No. 7/10 158-68, 2 figs. [19 refs.]

The author has shown that the serum of latently infected chickens which have been subjected to repeated injections of chicken blood heavily infected with *P. gallinaceum* contains antibodies in sufficient amount to give rise to a passive immunity in chickens which have been injected with it. This passive immunity is exemplified by the delay in the appearance of parasites in the blood after inoculation, and the lowering of the intensity and the curtailment of the resulting infection. When such immunized chickens are subjected to superinfection, not only is there a failure of parasitic forms. Similarly but there is also no new development of exoerythrocytic forms. Similarly when a blood relapse is caused by splenectomy this is not associated with the reappearance of exoerythrocytic forms. It seems clear therefore that the immune bodies in the serum are directed against both the erythrocytic and exoerythrocytic stages of the parasite. The question arises as to whether there is only one immune body capable of checking the development of both stages of the parasite or whether two distinct bodies are involved.

To settle this question, an attempt was made to liberate into the blood stream any immune bodies which might exist in the reticulo-endothelial cells, and which might be supposed to be immune bodies having a special action on the exoerythrocytic stages which develop in these cells. Accordingly chickens with latent malarial infection whose blood serum was shown to be devoid of any immunizing properties, were subjected to repeated injections of manganese chloride. This had the effect of conferring on the blood immunizing properties which it did not previously possess, as a result it is concluded, of the liberation of immune bodies from the reticulo-endothelial cells. These properties differed in no way from those possessed by the serum of chickens immunized by the repeated injection of heavily infected blood as in the first experiments. It seems clear therefore that the immune bodies produced by the stimulus of erythrocytic forms of the parasite are not different from those appearing in endothelial cells under the stimulus of the exoerythrocytic stages of development. As exoerythrocytic forms occur in the endothelial cells of the blood vessels as well as in cells of the reticulo-endothelial system in the tissues the further question arises—are the parasites in these two situations identical as regards their susceptibility to the immune substances in the blood, or are there differences between them which might have some bearing on the fact that sporozoite-induced malaria in man is liable to repeated relapse while blood-inoculated malaria is not?

G. M. Wemyss.

WOLFSON, FRANK. Effect of Preservation by Freezing upon the Virulence of *Plasmodium* for Ducks. *Amer J Hyg* 1945 Sept., v 42, No. 2, 155-68

The paper describes the results of experiments designed to test the degree of survival of three species of avian malarial parasite (*P. cathemerium*, *P. lophurae* and *P. trichaceum*) when blood taken from infected ducks is subjected to rapid freezing and, following storage at  $-76^{\circ}\text{C}$ . for periods varying from two hours to

one year to rapid thawing at  $42^{\circ}\text{C}$ . The effect of these procedures was estimated by the study of Giemsa stained films of the stored blood and by the results of inoculation into young ducks. It was found that the proportion of erythrocytes and probably of parasites which survived varied directly with the proportion of parasitized erythrocytes in the sample of blood before freezing. This is contrary to the findings of MANWELL and EDGETT in similar experiments. They stated that the greater the number of parasites in the blood the greater was the proportion of erythrocytes destroyed [this *Bulletin* 1944 v 41 189]. The author of the present paper found that the preservation of *P. cathe-merium* had no effect on the length of the prepatent period, the day on which the peak of parasitaemia occurred and the degree of the parasitaemia at the peak. The three parasites investigated showed no appreciable differences in their ability to survive as judged by the number of erythrocytes and parasites surviving, but the results of the infectivity tests indicated that *P. cathe-merium* survived more regularly than the other two parasites. It was noted that ducks inoculated from those infected from the frozen material developed a lower degree of parasitaemia than did controls but that from one to three subsequent passages were usually sufficient to restore the virulence of the parasite.

C. M. Wenyon

MARVIN H. N. & RIGDON R. H. Terminal Hypoglycaemia in Ducks with Malaria. *Amer J Hyg* 1945 Sept. v 42 No 2 174-8 2 figs. (12 refs.)

A study of the blood sugar level in ducks infected with *Plasmodium lophurae* has shown that there is an increasing hypoglycaemia following the peak of infection. At the time of death, usually 8 hours after the peak, there may be a 60 per cent. reduction in the blood sugar. As malarial parasites require relatively large amounts of sugar for their development *in vitro* it seems reasonable to suppose that the fall in the parasitaemia is the direct result of the hypoglycaemia. This is supported by the observations made by HEGNER and MACDOUGALL [this *Bulletin* 1926 v 23 863] that a hypoglycaemia caused by injections of insulin brought about a decrease of malarial parasites in canaries. According to the authors the course of events in these malarial infections in ducks is an anaemia caused by destruction of erythrocytes leading to anaemia. This damages the liver with impairment of hepatic function and hypoglycaemia which contributes to the death of the host in spite of the fact that it brings about a decrease in the parasitaemia.

C. M. Wenyon

RIGDON R. H. *Plasmodium lophurae* Infection of the Chick Embryo. *Amer J Hyg* 1945 Sept. v 42, No 2 169-94

The author has studied the results of inoculation of *Plasmodium lophurae* from infected ducks and chicks into developing chicken eggs. The results indicate that infection will not occur in embryos when infected blood is injected into the yolk sac. Infections on the other hand, will result if the blood is inoculated directly into the embryo. If such inoculated embryos are allowed to hatch, it will be found that usually few if any parasites are present in the blood. In only one chick was there a high grade parasitaemia at the time of hatching. More often parasites first appeared in the peripheral blood on the third or fourth day after hatching and the degree of the resulting parasitaemia varied. Some chicks showed only a few parasites on several days while others developed a high degree of parasitaemia. It appears from this study that the chick embryo is not such a suitable host for *P. lophurae* as the young chick. Some unknown factor in the embryo appears to hinder its development. No significant pathological lesions were observed in the infected embryos except

MARTINS A. V., VERSIANI V. & TUPINAMBÁ, A. A. Estudos sobre a moléstia de Chagas no estado de Minas Gerais. I. Estudo epidemiológico de um foco da moléstia no município de Jaboticatubas. [Chagas's Disease in the State of Minas Gerais. I. Epidemiological Study of a Focus in Jaboticatubas.] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais* 1945 v 1 51-61 12 figs. on 9 pls. English summary (10 lines)

This investigation was carried out at the end of 1939 and the beginning of 1940 and was cut short by the death of Evandro Chagas. Jaboticatubas is a small municipality in central Minas Gerais, some 70 kilometres from the capital. The inhabitants live in hovels (*casas*) some with mud walls, made of woven twigs and laths the interstices being filled with earth, others with uncelled tile roofs. The district is fairly dry and relatively healthy there is no malaria, but infestation with *Ascaris lumbricoides* is very common. The inhabitants live by cultivating millet and manioc, and, to a small extent on the lower levels rice.

Of 18 mud huts investigated, 15 were harbouring the vector of *T. cruzi* and the insects were found infected in 9 of them. Only one of the tiled huts was infested and the insect caught was positive for *T. cruzi*. Of a total of 146 inhabitants 33 were found positive by examination of thick drops and by xenodiagnostic methods. In 10 of the 18 mud huts the inhabitants were positive, and in 7 of the tiled huts. In the former the inhabitants totalled 102, and 23 of them were infected in the latter 44 and 10 were infected. Of the 33 infected, 15 were in the second decade none was under one year of age. There was no appreciable difference as regards sex 14 of 66 males were infected and 19 of 80 females.

Animals were also examined. Of the domestic animals 5 of 22 dogs and 2 of 7 cats were infected all 7 were in the mud huts none in the tiled. Forty wild animals belonging to 9 species were examined, but only two armadillos (*Dasyurus novemcinctus*) were positive. Of 124 *Paratrypanosoma megistus* examined 36 were positive and 7 of 51 *Triatoma sordida* that is 43 were positive out of a total of 175 vectors examined. There are 12 photographs showing clearly the terrain and the inhabitants.

H. Harold Scott.

MARTINS A. V., VERSIANI V. & TUPINAMBÁ, A. A. Estudos sobre a moléstia de Chagas no estado de Minas Gerais. II. Sobre 156 xenodiagnósticos feitos em Belo Horizonte. [Chagas's Disease in the State of Minas Gerais. II. One Hundred and Fifty-Six Xenodiagnostic Tests carried out in Belo Horizonte.] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais* 1945 v 1 63-70 1 folding map English summary

Xenodiagnosis has proved to be the most reliable test in chronic cases of Chagas's disease. The subjects selected for the test were attending the hospitals and clinics in Belo Horizonte Minas Gerais Brazil. The investigation was carried out at intervals between April 1939 and August 1942, and the subjects chosen came under one or other of four categories i. With myocarditis of undetermined cause ii. With mal de encaço (mega-oesophagus) [see this Bulletin 1921 v 18 301 1927 v 24 830]. iii. With gutta serena with or without cretinism. iv. Those with no definite symptoms but presenting themselves for examination either because they lived in places where Chagas's disease is endemic, or because others of their families were suffering from it.

The insects used were *P. megistus*, *T. infestans* and *T. triticeus* reared in the laboratory. They were examined 40 days after their feeding on the patient their rectal contents taken by pipette and later their whole bodies were dissected and examined.

Generally one test only was made with each patient. The results were as follows. Of 63 in Group i (myocarditis patients) 23 were positive of 48 in Group ii (mega-oesophagus) 22 positive of 28 in Group iii (goitre) 5 positive and all came from parts of the State where infected bugs had been captured. Of Group iv one was positive out of 17. In all 51 were positive among the 156 tested. The distribution in the 32 municipalities is given but this is not of much value since none gave more than 3 and 18 had only one each. 9 had two.

H Harold Scott

VIZCARRONDO R. O. Notas sobre la enfermedad de chagas y en particular en el Estado Aragua. [Notes on Chagas's Disease, especially in the State of Aragua.] *Rev Sanidad y Asistencia Social* Caracas. 1945 Oct.-Dec. v 10 Nos 5/6 635-66 1 map & 15 figs. on 10 pls [41 refs.]

As usual in articles on Chagas's disease the opening pages repeat the history of Carlos Chagas's early work, the vectors of infection and the modes of conveyance. After this the author shows on a sketch map the places where infected *Rhodnius* were found but in 7 chief districts only 107 insects were examined 48 were found positive. Next examinations were made of inhabitants of the town of Maracay. Eight per cent. of schoolchildren had palpable spleens and 6 per cent. harboured malaria parasites the corresponding figures for soldiers were 13 and 11 per cent. and for various people in the town 4 and 6 per cent. [These figures convey little if any useful information since in no case is the number examined stated.] Then follow descriptions of three cases. The first is called a case of lymphatic leukaemia with leucopenia seemingly because there was a relative lymphocytosis. Red corpuscles numbered 1,300,000 white 1,600 per cmm. lymphocytes 42 per cent. Ova of *Accator americanus* and of *Trichuris trichiura* were found in the stools and the case would appear to have been one of helminthic infestation with secondary anaemia. Malaria parasites were repeatedly looked for but in vain. The second was a case of myelocytic leukaemia the third had some degree of anaemia and xenodiagnosis proved infection by *T. cruzi*. Other notes include a chemical analysis of the water of Lake Tacarigua made in 1941 and research on the use of DDT its pharmacological action and its compatibles.

H Harold Scott

LIEM S. D. & VAN THIEL, P. H. The Complement-Fixation Test for Chagas' Disease employing a Dried Culture Antigen. *Acta Leidensia (Scholae Med Tropicae)* 1940-41 v 15-16 259-74

Tests of a dried antigen prepared from a culture of trypanosomes on horse blood glucose agar [see LIEM this *Bulletin* 1938 v 35 719] are described. The strain of trypanosomes was isolated at Hamburg in 1935 by MALAMOS [*ibid* 1935 v 32 718] from *Macaca irus* [*Macacus cynomolgus*] recently arrived from the Netherlands East Indies. It was identified by Malamos as *T. cruzi*. The authors received the strain in the bug *Triatoma infestans* in 1936.

The sera of rabbits immunized by intravenous injections of cultures of the trypanosome and the sera of dogs infected with it were used for antibody while guinea-pig serum provided the complement. The sera of two persons in South America who were suffering from Chagas's disease were sent to the authors at Leiden, Holland, and gave negative results in the complement fixation test but owing to the time taken in transit no conclusion can be drawn from the tests. As a control, 385 sera of patients in Holland suffering from various diseases were tested. 4 out of 146 Wassermann positive sera were positive and 4 out of 6 sera of patients suffering from chancroid were also positive but all the other sera were negative.

The authors conclude that the dry antigen used, which is sealed *in vacuo* in ampoules and kept in the refrigerator is better than other antigens, and they recommend its trial in known cases of Chagas's disease in South America.

J. F. Corson

MAZZA, S. BASSO G. & BASSO R. Investigaciones sobre enfermedad de Chagas. Contribución para la terapéutica de la enfermedad de Chagas. Últimos ensayos quimioterápicos M.3024, I.C.I. Aplicación de penicilina. [Studies on Chagas's Disease. Treatment with M.3024 and with Penicillin.] Universidad Buenos Aires Misión de Estudios de Patología Regional Argentina (Jujuy) Publicación No 70 1945 81 pp. 36 figs. [Bibliography]

The authors begin by reviewing the literature on the use of 7602 (Ac) Bayer in Chagas's disease and follow this by a record of cases in which they have used M.3024 the British equivalent of the Bayer preparation. Several of these cases are detailed. The initial dose is 7-12 mgm. per kilo body-weight usually 0.15 gm. 2-4 cc. were generally given at 6-7-day intervals, the second dose being double that of the first. Improvement was rapid and the external signs (swelling of the eyelids and face) disappeared in 5-12 days.

Penicillin was then tried. It was given by intramuscular injection 2 cc. every 3 hours containing 3 000 Oxford units per cc. Again several cases are detailed and the total amount given was about 400 000-500 000 units. Both local and systemic symptoms improved. [The authors do not attempt to discuss the relative values of these forms of treatment. It would be instructive if they would present parallel series of cases and a reasoned discussion of the results observed.]

H. Harold Scott.

### LEISHMANIASIS

GEVORKOV A. A. Incidence of Visceral Leishmaniasis in Samarkand during 20 Years (1924-1944). *Med. Parasit. & Parasitic Dis.* Moscow 1945 v 14 No. 3 88-9 [In Russian.]

The author analyses the incidence of visceral leishmaniasis in Samarkand (Middle Asia) from 1924 to 1944. During this period the total number of recorded human cases was 921 which were fairly evenly distributed from year to year in spite of a progressive increase in the population in the course of 20 years. Thus, the absolute growth of the population was not accompanied by a proportional rise in the incidence of kala azar. A comparison of the figures for the incidence of leishmaniasis in man and in dogs for 11 years (1933-43) shows that there is a complete parallelism between the two diseases: the fluctuation in the incidence of human disease corresponding to that in the canine and being correlated not only with the percentage of infected dogs but also with the total number of dogs in the town.

As regards incidences in age-groups, the great majority of cases (54-74 per cent. of all cases) occur in children between the ages of one and five and chiefly from one to three. Children older than ten years are rarely affected, while during the last nine years there has not been a single case of infection in persons older than 18 years.

It is concluded that the stabilisation of the incidence of kala azar in Samarkand is due to the systematic measures adopted for the early diagnosis and treatment of the disease as well as to the elimination of infected dogs. The latter are regarded as constituting the chief epidemiological danger.

C. A. Hoare

JUNG SUN C. Kala-Azar in Lanehow and its Vicinity *Chinese Med J* (Chengtu Edition.) 1944 Oct. v 63A, No 1 12.

MUNTER E J & PACKCHANIAN A. Two Exogenous Cases of Visceral Leishmaniasis (Kala-Azar) in the United States with Notes on Cultivation of *Leishmania donovani* In Vitro *Amer J Trop Med* 1945 Nov v 25 No 6 507-12 4 figs. [12 refs]

The cases reported were in native Indian seamen from Assam where the disease was contracted. Diagnosis was established by the discovery of leishmania in smears of bone marrow and in cultures made from the bone marrow and the peripheral blood. Various serological tests were also positive

C M Wenyon

NAJERA ANGULO L. Observaciones sobre el ciclo evolutivo de *Leishmania infantum* Nicolle 1908 [The Developmental Cycle of *Leishmania infantum*] Reprinted from *Rev Ibérica de Parasit* Granada. (Tomo extraordinario) 1945 Mar 181-98 1 fig & 1 coloured pl. [22 refs.]

In this paper the author upholds the view as others have done that the parasite of infantile kala azar may reproduce by schizogony. The majority of observers believe however that the appearances of schizogony are due to the presence of leishmania in detached portions of the cytoplasm of infected macrophages in which the outlines are not visible owing to bad fixation or degenerative changes. In the present paper the author suggests that certain granular cytoplasmic bodies seen especially in smears of the bone marrow of cases of infantile kala azar and which contain no semblance of the characteristic leishmania nuclei and kinetoplasts are actually young schizonts. They are described as increasing in size till they are larger than a red blood corpuscle. Associated with this growth there are gradually formed in the cytoplasm presumably from the granules a series of nuclei and kinetoplasts. Finally by separation of cytoplasm around the nuclei and kinetoplasts a varying number of leishmania are formed, which lie in a cyst membrane the remains of the supposed schizont. These leishmania are liberated by rupture of the cyst and either commence the process again or are phagocyted by the macrophages. These phagocyted leishmania may fill the macrophages and have hitherto been regarded as parasitic in these cells. According to the author they are destined for phagocytic destruction. What is perhaps most remarkable is the author's opinion that this type of development is peculiar to *Leishmania infantum* and will account for the differences in the diseases caused by this parasite and *L. donovani*. The paper is illustrated by black and white text figures and a coloured plate which the reviewer has to admit he finds unconvincing.

C M Wenyon

ADLER, S. The Sandflies of Cyprus (Diptera) *Bull Entom Res* 1946 Feb v 36 Pt. 4 497-511 6 text figs & 4 figs. on 1 pl. [24 refs]

Ten species of *Phlebotomus* were collected in Cyprus during August and September 1944. They were *P. papatasi* *sergenti* *alexandri* *perniciosus* var *tobbi* *chinensis* *perfulvipes* *larroussesi* *parroti* *arisi* sp. n. and *fallax* var *cypricola* var nov.

Taxonomy of these species is discussed and the new forms are described and illustrated. Keys to both sexes are provided.

The incidence of human visceral leishmaniasis in the island is unknown though the first case was recorded in 1935. Canine kala azar is not rare. The author considers that *P. perniciosus* var *tobbi* and a race of *P. chinensis* should be investigated as possible vectors.

H S Leeson



CHATTERJEE H. V. Postmortem Femoral Bone Marrow Studies of Kala-Azar  
*Trans. Roy. Soc. Trop. Med. & Hyg.* 1946 Feb., v 39 No. 4 315-20  
 4 figs. on 1 pl. (13 refs.)

An examination of the femoral bone marrow from fatal cases of kala azar has shown that in an acute case there was almost complete absorption and replacement of the fat cells. There was a total absence of the degenerative changes met with in later stages of the disease the general structure of the marrow being made up of large numbers of clasmotocytes and cells of the myeloblastic series. Of the clasmotocytes about 30 per cent. contained leishmania. In later subacute cases the marrow reddish in colour was tougher than normal. The total number of cells was diminished particularly in certain areas which contained few cells and presented a homogeneous ground-glass-like appearance. Of the clasmotocytes present, nearly all contained leishmania. The ground-glass-like material was the result of precipitation of fine fibrils in the fat vacuoles. In addition there was some increase in the argyrophil reticular fibres. In later chronic cases there was a further reduction in the number of cells, those of the myeloid series being remarkably diminished. The reticulo-endothelial cells of clasmotocytes were the most conspicuous cells. They possessed a large amount of amoeboid and branched protoplasm and were packed with parasites. The fibrils noted in the subacute cases were more pronounced, while there was a marked proliferation of the argyrophil reticular fibres. The author concludes that the progressive degeneration of the marrow and the cellular changes will explain the leucopenia and neutropenia and increasing anaemia which are characteristic of kala azar. C M Wenyon.

GELLERSON A. VAN DYKE, H. B. PYLE & J. TUPIKOVA, N. A. Amyloidosis in Hamsters with Leishmaniasis. *Proc. Soc. Exper. Biol. & Med.* 1946 Jan. v 61 No. 1 25-30 3 figs.

In a recent paper GOODWIN [this Bulletin 1946 v 43 316] has shown that hamsters infected with *Leishmania donovani* may suffer from oedema nephritis proteinuria and depression of the level of the plasma proteins. The authors of the present paper confirm these findings and give the additional information that, on and after the 46th day of the infection an increasing degree of amyloidosis occurs in various organs more particularly in the kidneys and suprarenals. At the same time it was noted that though the globulin level in the blood remained normal the albumin level fell considerably so that the A/G ratio was significantly lowered in the infected animals. This decrease in the blood albumin was correlated with the passage through the kidneys of increasing amounts of albumin due to the amyloid degeneration of the glomeruli and to a lesser extent of the tubules. At the same time there was a lowering of the colloid osmotic pressure of the plasma leading to the escape of excessive amounts of fluid into the tissues and to the development of oedema and anasarca. The authors do not believe that failure of the synthesis of plasma albumin is responsible to any important extent for the lowering of the percentage of this protein in the plasma. C M Wenyon.

SEN GUPTA, P. C. 4 4 Diamidino-Diphenyl-Ether in the Treatment of Indian Kala Azar. *Indian Med. Gaz.* 1945 Oct. v 80 No. 10 495-8.

In an earlier communication [this Bulletin 1945 v 42, 264] the author reported upon the treatment of 16 cases of kala azar with this drug, which has been given the proprietary name of phenamidine (M & B 736). In the present paper these 16 cases together with 14 others similarly treated are considered. The ages varied from 1 to 80 years and the duration of illness from

1 month to 2 years. The drug was administered intravenously in 1 per cent solution the usual course being one injection each day for 10 days. This was followed by a second course after a 10-day interval. The initial dose for an adult was 25 mgm. This was increased by 25 mgm. daily till a dose of 1 mgm per pound of body weight was reached. The mean total dose for an ordinary case worked out at  $1.73 \text{ gm.} \pm 0.477 \text{ gm.}$  or for 100 pounds of body weight,  $1.854 \pm 0.396 \text{ gm.}$  Of the 30 patients 24 completed the treatment and were discharged as clinically cured. Six months later 21 of these were traced. Sixteen were in good health and were considered cured, while five had relapsed. The permanent cure rate is given as  $64 \pm 19$  per cent. It is concluded that the drug is inferior to the most effective pentavalent antimonials or to diaminodistilbene. On the other hand it is non-toxic and should be useful in cases in which antimonials are contraindicated as for instance when the complication of grave pulmonary tuberculosis exists.

C M Wenyon

WIEN R. Excretion of Stilbamidine *Trans Roy Soc Trop Med & Hyg* 1946 Apr v 39 No 5 455-8

Stilbamidine was injected subcutaneously into rats in doses of 1 to 10 mgm. per kgm every day for 15 days and the excretion in the urine was measured by means of the fluorescence (which measures the unchanged molecule) and by a glyoxal reaction (which measures both the unchanged and slightly changed molecule). With a daily dose of 1 mgm. per kgm the percentage excretion of the day's dose was 1.6 on the 5th day 1.8 on the 10th day and 2.5 on the 15th day when measured by the fluorescence and 42 on the 5th day 52 on the 10th and 59 on the 15th day when measured by the glyoxal method. A large proportion of stilbamidine was presumably metabolized and excreted in a non-fluorescent form. Similar results were obtained when the excretion of 2-amino-4,4-diaminodistilbene was studied. This compound is closely similar to stilbamidine (4,4-diaminodistilbene) but it can be estimated by diazotization as well as by fluorescence. The greater the number of injections of stilbamidine which had been given the higher was the proportion of the daily dose excreted. Conversely the larger the daily dose the smaller was the proportion excreted, presumably the kidney could eliminate only a limited amount of the compound. The higher doses (5-10 mgm. per kgm.) were toxic, and some of the animals died.

F Hawking

PACKCHANIAN A. Leishmaniasis. The Cultivation of *Leishmania tropica* from Two American Soldiers who had returned to the United States from the Near East *J Amer Med Ass* 1945 Oct. 20 v 129 No 8 544-7 [Refs. in footnotes]

The paper is based on two cases of oriental sore in soldiers returned to the U.S.A. from Iran. In both cases parasites were demonstrated in the lesions while cultures in the water of condensation of blood agar medium were obtained. Attention is called to this occurrence of exogenous cases of oriental sore in the U.S.A. and a warning is issued that further cases of the kind may be expected. The author advises the making of cultures in all suspected cases for if a positive culture is obtained there is no danger of confusing the flagellates with other organisms whereas in smears from the sore inexperienced observers may confuse yeasts with leishmania and in consequence make an erroneous diagnosis.

C M Wenyon

KOJEVNIKOV P. V. [The Absence of Cross-Immunity between the Two Types of Cutaneous Leishmaniasis.] *Med. Parasit. & Parasitic Dis.* Moscow 1945 v 14 No 3 82-8. [In Russian.]

It is well known that cutaneous leishmaniasis usually conveys a lasting immunity though cases of reinfection are also known thus among 1,894 case histories in Ashkhabad the author found 86 (4.5 per cent.) records of repeated infections. Cases of reinfection are especially liable to occur on transfer from one endemic area to another. In 1940 the author established the presence in Middle Asia of two types of oriental sore the dry urban form and the moist rural form [see this *Bulletin* 1944 v 41 331]. On analysing the above 86 cases of reinfection it was found that 18 patients originally had the first form, later acquiring the second form while in four cases the sequence was reversed whereas in 62 patients the type of the original infection remained unknown. Moreover in some cases the two types of sores developed independently in the same subject. It was suggested that there was no cross-immunity between the two types of cutaneous leishmaniasis.

The author records further observations confirming this view. In 1942 a large group of schoolchildren from Ashkhabad, where the dry variety of oriental sore is prevalent spent one to two months on field works in an endemic area of the moist variety with the result that 59 per cent. of the children acquired an infection with the latter type of the disease. It was ascertained that of 300 children, 49 had formerly suffered from the dry form of the disease 10 had been vaccinated with this variety while two had previously had sores of the moist type. In 44 children there was circumstantial evidence of previous infection with the dry form, whereas in 45 no data were available. In 55 per cent. of the cases a previous infection with oriental sore of the dry type failed to protect against infection with sores of the moist type. However a previous infection with the former type reduced the severity of the second infection pointing to some degree of group immunity. Further confirmation of the strain-specificity of the immunity was provided by the results of vaccination inoculation of cultures of leishmania isolated from sores of one type protected against infection with the homologous sores but not against heterologous sores. Finally there is evidence that in rare cases, there may be reinfection after five to nine years with sores of the same type as in the primary infection.

It is concluded that cross-immunity between the two types of oriental sore absent or only slightly developed and that the course of infection with a homologous type is milder than in the primary disease. In prophylactic vaccination against cutaneous leishmaniasis either the strain used should correspond to the type of sore prevalent in the locality where the vaccinated person proposes to reside or strains of both types should be used.

C. A. Hoers

FILATOV V. P. Tissue Therapy in Cutaneous Leishmaniasis. *Amer. Rev. Soviet Med.* 1945 Aug. v 2 No 6 484-90 14 figs. on 2 pls.

Under the term tissue therapy the author describes a procedure which he states is based on a new principle in medicine. He holds that animal and plant tissues when preserved under adverse conditions generate biogenic substances which stimulate healing and regeneration when they are introduced into the body. The introduction may be made by various methods—grafting, implantation, subcutaneous and intramuscular injection, surface applications, rectal injections. The author claims that a great many diseases have been successfully treated by this method among these cutaneous leishmaniasis is

specially mentioned in this paper. This has been treated by grafting on to areas from which a piece of healthy skin has been removed a similar piece of skin which had been removed from a cadaver and had been preserved under refrigeration for a week. Within a few days of the skin graftings which are made at points distant from the sores changes occur in the leishmania ulcers and healing takes place in two to three months with a minimum of scarring. Similar results were obtained by grafting the preserved skin of the rabbit or by the injection of extract of the leaves of the aloe which had been preserved in the dark. The author concludes that the cases described in the paper demonstrate the powerful effect which tissue therapy exerts in cutaneous leishmaniasis. Grafting of conserved skin and subcutaneous injection of an extract of preserved aloe leaves are equally effective. Tissue therapy acts by virtue of systemic stimulation independently of the aetiology of an ulcerative process. Thus tuberculous ulcers, syphilitic ulcers and leishmania ulcers are equally benefited. The paper is illustrated by a series of photographs showing the results of treatment of leishmania ulcers by the author's method.

C M Wenyon

### FEVERS OF THE TYPHUS GROUP

ROY B C Typhus Fever with special reference to its Incidence in India  
*J Indian Med Ass* 1946 Feb v 15 No 5 135-46 149 2 figs. (1 map)  
[89 refs.]

In this clinical description the author uses the name typhus fever as synonymous with the term fevers of the typhus group and he seems to favour the unconventional view that all the fevers of the group in India are louse-borne. He states for example that it has not been proved of course that Indian typhus is louse-borne but there is no reason to suppose the contrary. Blood of various arthropod vectors was examined but no definite clue could be obtained.

The paper contains a good deal of useful information including a table showing the localities in India from which cases have been reported up to 1943 also the vector suggested in each group of cases and the serological type when this has been recorded. There is a bibliography which gives references to most of the articles dealing with typhus-group fevers in India up to 1943 but no reference is made to the important observations published since that date.

John W D Megaw

PLOTZ H WERTMAN K. & BENNETT B L. Identification of Rickettsial Agents Isolated in Guinea Pigs by means of Specific Complement Fixation  
*Proc Soc Exper Biol & Med* 1946 Jan. v 61 No 1 76-81

The experiments described in this paper show that the complement-fixation test as applied by the authors is the most reliable method of differentiating the rickettsiae of murine typhus, epidemic typhus and Rocky Mountain spotted fever in guinea-pigs. The special proviso is that the antigens employed must be purified by washing to remove the common antigen.

The results of the experiments are shown in three tables from which the following analysis has been prepared to show the trend of the responses observed in three lots of guinea-pigs each of which received intraperitoneal injections of equal doses of one of the strains of rickettsiae. The data refer to the animals that survived all causes of death long enough to allow the fixation test to be carried out about four weeks after inoculation.

Strain of Infection	In cuba tion (days)	Fever (days)	Scrotal Reaction		Complement-fixation titre		
			Pre- sent	Ab- sent	Epi- demic	Murine	R.M.S.F
Murine (Wilmington)	3-7	0-7	31	11	0-80	80-640	0
Epidemic (Breml)	5-19	0-10	4	35	80-640	0-40	0
R.M. spotted fever (mild strain)	2-6	2-6	No mention		0	0	320-640

Some cross-fixation occurred in many of the guinea-pigs inoculated with epidemic and murine strains but in every case the titre with the homologous antigen was at least four times as high as with the heterologous. There was no cross-fixation between Rocky Mountain spotted fever and the other two infections.

Two of the 42 guinea-pigs inoculated with murine rickettsiae had no febrile reaction but their sera yielded homologous fixation titres of 1-160 and 1-320 and immunity tests showed that they had reacted with inapparent infections.

Six of the 39 guinea-pigs infected with epidemic rickettsiae had no febrile reaction one of these had a fixation titre of 1-160 and was proved to be immune the other five remained negative to the test and were non-immune so they must have escaped infection.

The consistent reliability of the complement fixation test in the differential diagnosis of the type of infection in inoculated guinea-pigs is in striking contrast with the uncertain indications yielded by the febrile and scrotal reactions.

[Further investigation will be needed to show whether all strains of these types of rickettsiae can be expected to give equally consistent responses.]

*John W D Megaw*

GROUP V & DOVONICK R. On the Specificity of Epidemic and Murine Typhus. *Science* 1946 Mar 16 330-31

The existence of specific differences between epidemic and murine typhus fevers has been shown by the following experiments.

Two groups of young Swiss-white-mice were vaccinated one group with epidemic vaccine of the Breml strain, and the other with murine vaccine of the Wilmington strain. Fourteen days later half of the mice of each group were challenged by lethal doses of toxins obtained from epidemic rickettsiae and the other half by corresponding doses of murine toxins. The results observed 18 hours later were —(1) Of 23 mice vaccinated by epidemic vaccine 20 survived the dose of epidemic toxin whereas all the 23 vaccinated by the same vaccine and challenged by murine toxin died. (2) Correspondingly of 23 mice vaccinated by murine vaccine 22 survived the dose of murine toxin, whereas all the 23 vaccinated by murine vaccine and challenged by epidemic toxin died.

These findings are opposed to those reported by FITZPATRICK, who obtained results suggesting that the epidemic and murine toxic factors are identical [this *Bulletin* 1945 v 42, 783]

*John W D Megaw*

DICK J C. Notes on the Weil-Felix Reaction in Typhus Fever and other Diseases. *J Path & Bact* 1946 Jan. v 58 No. 1 21-30 [24 refs]

Between March 1942 and February 1944 505 Weil-Felix tests were carried out on 308 cases of various fevers including 80 of typhus in a hospital in the

Middle East Standard R.A.M.C. suspensions and Dreyer's tubes were used. The results were read after overnight incubation at 37°C. The end point was the last tube in which a definite ring of particles could be obtained by rotation and seen by the naked eye at the neck of the tube with examination in a strong light against a dark background. In these conditions within the first 10 days of illness a titre of 1-240 was regarded as slightly suggestive of typhus and one of 1-480 as very suggestive. At any stage a titre over 1-480 was considered as definitely positive.

At first all the three usual strains of *Proteus* were used but it was soon found that non-specific reactions with OXA were relatively common at titres of 1-480 and even titres of 1-960 with this strain could not be regarded as definitely positive so that in the absence of evidence of the existence of mite borne typhus in the area the OXA test was discarded.

In 68 of the 80 cases of typhus fever rickettsia-agglutination tests were carried out by VAN ROOYEN who diagnosed 21 of them as epidemic (house borne) 36 murine (flea-borne) and 11 as incapable of being differentiated by the test.

Among the 80 cases of typhus the Weil-Felix titre (OX19 or OX2 or both) rose to above 1-480 in 73 and to 1-480 in the remaining seven. The earliest definitely positive reaction occurred on the 6th day and in observations made after the 10th day the titre fell below 1-480 in only two cases both of which yielded titres above 1-480 at a later date.

The titre with OX19 was usually higher than that with OX2 but in six murine cases and one other the positive titre was reached with OX2 and not with OX19.

No evidence clinical or bacteriological could be found to warrant the claim that the cases of OX2 agglutination studied were due to tick borne infection. [The possibility that tick typhus might occur in M.E.F. and Egypt was suggested by the reviewer who stated that it would be surprising if the tick borne disease were absent from the area which included Egypt Palestine and parts of Iraq and Persia (this *Bulletin* 1945 v 42 195).]

Among 26 cases of typhoid fever titres of 1-120 or over were observed in nine patients and in three of these the titre with OX2 reached 1-240. Among 28 cases of paratyphoid A or B a titre of 1-240 was reached in eight. In one patient with paratyphoid B a double infection was considered possible because the titre with OX19 and OX2 was 1-960 on the 14th and 16th days and by the 90th day the OX19 titre was 1-60 and the OX2 titre was 1-30 all the other evidence however was opposed to the existence of typhus infection in this case. In two cases of paratyphoid A titres of 1-240 with OX19 and 1-120 with OX2 were observed on the 5th and 8th days respectively but by the 27th and 32nd days the titres had fallen to 1-30. Rising titre agglutinations at low levels occurred with OX2 in typhoid and with OX19 and OX2 in paratyphoid in some cases so the author advises that care should be exercised in the interpretation of such reactions.

In 166 cases of fevers other than typhus and the enteric group 268 Weil-Felix tests were carried out at various stages. In 22 cases no agglutination occurred in 80 the maximum titres with OX19 or OX2 or both were 1-30 or 1-60 in 52 the maximum titre was 1-120 in 10 it was 1-240 and in two it was 1-480. Titres of 1-60 or under are regarded as insignificant. In most of the non specific agglutinations with titres of 1-120 or over the highest titre was usually observed early and a fall soon occurred but sometimes the titre remained fairly constant and in a few cases a rising titre was observed. Non specific agglutination was more frequent with OX2 than with OX19.

Among six cases of measles three reacted at 1-120 with OX2 and a fourth had a titre of 1-480 up to the 7th day after which the titre fell. One case of

common cold gave a titre of 1-480 (OY2) and two of influenzal broncho-pneumonia reached 1-240 (OY2). In two of eight cases of infective hepatitis a titre of 1-120 (OY19 and OX2) was observed in the later stages. In several cases of pyrexia of unknown origin repeated tests were made the titre never arose above 1-250. In a case of lymphadenoma the findings were confusing as can be seen from the table below —

Day of disease	Agglutination titres				
	OX19	OY2	OXK	Epidemic rickettsiae	Endemic rickettsiae
13	0	0	480	0	500
27	60	240	960	0	500
64	60	120	480	0	200

In a case of tonsillitis with an irregular rash, in which diphtheria occurred as a complication on the 16th day the titres with OX19 and OX2 were — 6th day 1-30 14th day 1-120 and 23rd day 1-240. In a case of dysentery with indefinite exudate the OX19 titre was 0 on the 3rd day and 1-120 on the 8th day.

Attacks of murine typhus occurred in two persons who had been inoculated against typhus six and eight weeks previously. In both, the Weil-Felix reaction developed in the usual way. So also in five inoculated persons who suffered from fevers other than typhus the agglutination responses did not differ from those occurring among uninoculated persons in otherwise similar conditions.

The author suggests that the non specific reactions may have been due to previous inoculation with T.A.B. vaccine and tetanus toxoid, which had been received by all the patients in the series and which appear to have had some effect in activating the patient's shadow factories for manufacturing agglutinins. The great majority of the patients were British and none of the others had come from places where typhus fever was endemic.

John W. D. Megaw

ANDREWS, C. H., KING, H. & WALKER, J. Chemotherapeutic Action of Dyes in Typhus Infection of Mice. *Brit J Pharmacol* 1946 Mar., v 1 No. 1 15-20

This important paper is published in the first number of the *British Journal of Pharmacology and Chemotherapy* which makes a welcome though belated, appearance. Some points of general interest are as follows — Among the substances already found therapeutically active in typhus infection of mice are methylene blue, toluidine blue and other dyes of the thiazine group. The authors with VAN DEN ENDE, had already carried out routine tests of methylene blue and toluidine blue on infected mice but had failed to find any benefit, presumably, because the drugs were badly tolerated when administered by the peritoneal route employed in the experiments. These and some other dyes have now been tested on mice infected by the nasal route according to the technique already described by the authors [*this Bulletin* 1945 v 42 20]. Various doses of methylene blue and toluidine blue were administered to the mice (1) mixed with their food (2) by the oesophageal route using measured doses and (3) subcutaneously. Both dyes in suitable doses completely suppressed the development of lung lesions when administered by any of these methods. A murine strain of rickettsia was used, but in two tests of toluidine blue epidemic rickettsiae were employed, and the results were rather less satisfactory.

A large number of dyes were tested for *in vitro* activity by mixing suspensions of murine rickettsiae with solutions of the dyes keeping the mixtures at room temperature for 45 minutes and then injecting them intradermally into the shaved skin of rabbits. It was found that methylene blue toluidine blue six other dyes of the thiazine group and selenium methylene blue in dilutions of 1-500 000 prevented the development of the Girond reaction. Various acridine dyes including proflavine acriflavine and atebrin were ineffective in strengths of 1-2,000. The results of this test do not always agree with those obtained with the mouse test for example the drugs V 147 and "V 188" which had already been found by the authors to be more effective than methylene blue or toluidine blue in the treatment of mice showed no activity when subjected to the rabbit intradermal test.

PETERSON had already shown that toluidine blue inactivated murine rickettsiae *in vitro* and also had a therapeutic action when administered to infected mice with their food [this *Bulletin* 1944 v 41 935].

Mention is made of the successful treatment of typhus-infected mice with methylene blue by KIRUTH and SCHILLING [*Zent f Bak* 1 Abt. Orig. 1944 v 151 293].  
*John W D Megaw*

SACHS A. Typhus Fever in Iran and Iraq, 1942-43. A Report on 2,859 Cases. *J Roy Army Med Corps* 1946 Jan. & Mar v 86 Nos 1 & 3 1-11 87-108 14 figs on 3 pls. 2 graphs & 7 charts. [17 refs.]

[This report will supply valuable material for the typhus-fever chapter of the medical history of the recent war. In the present abstract it is possible to deal with only a few of the interesting observations recorded by the author.]

The disease among British and Indian troops in the area during 1942-43 conformed closely in most respects to the pattern seen in the Mesopotamia campaign during 1917-18 even the case-fatality rate (21.9 per cent.) was much the same as in the previous war when it was 22.75 per cent.

Considering the degree of exposure to infection the incidence among the troops was low—0.78 per mille during the first seven months of 1943. Disinfection with the powder A.L. 63<sup>1</sup> containing derris and naphthalene was regarded as giving satisfactory results. A Cox type vaccine was available for about one fourth of the troops including some exposed to special risk. Among the vaccinated subjects the incidence was 0.37 per mille among the unprotected it was 0.91 per mille. Only two deaths occurred among the 51 000 protected against 33 among 155 000 unprotected. No attacks occurred later than six weeks after the third dose of vaccine had been given.

Sulphapyridine was given to 336 patients but even when the administration was started before the fifth day there was no reduction in the incidence of bronchopneumonia or in the fatality rate.

The clinical features of the disease were similar to those usually noted in outbreaks of a corresponding kind but a curious observation was that in 55 per cent. of the fatal cases in North Iran death was attributed to circulatory failure or pulmonary oedema whereas in South Iraq these conditions were not reported as having occurred in any case. In one group of 60 cases acute abdominal symptoms occurred in three patients one of whom recovered after an exploratory operation the other two died one of them two weeks after an operation for appendicitis and the other without surgical intervention. In these two fatal cases haemorrhages into the wall of the caecum and massive sub-pericardial haemorrhage were found after death.

The morbid histology of the disease was closely studied, and the characteristic vascular lesions were found but in addition to the usual typhus nodules associated with the small vessels of the brain there were also nodules in the



brain which had no apparent connexion with the vascular system. The detailed description of the microscopic changes is illustrated by 14 good photomicrographs and in three of these rickettsiae are shown. For the demonstration of rickettsiae a slight modification of Wolbach's technique was employed — after fixation of the tissues for 24 hours in Zenker's fluid, paraffin sections were cut and treated with xylol ether and various dilutions of alcohol. The sections were stained for 12-18 hours in a mixture consisting of — distilled water 100 cc. 0.5 per cent. sodium bicarbonate solution 2-4 drops methyl alcohol 3 cc. and Giemsa's stain 2.5 cc. Differentiation was by acetone.

A Weil-Felix titre with *Proteus* O19 rising rapidly to 1-100 or more was regarded as suggestive. The percentage of sera in which titres of 1-1 000 or over were reached in the second week was about 30 among British and Indian troops but only about 9 among Iranian civilian patients. In the fourth week the figures were even more strikingly different 50 per cent. and 8 per cent. respectively. On the other hand, titres of 1-100 or over were reached by the 5th to the 7th day in 50 per cent. of the civilian patients and in only 24 per cent. of the military cases.

*Proteus* O12 was agglutinated at titres equal to or higher than, those obtained with O19 in 10 per cent. of the sera from Iranian patients examined.

In a series of 81 sera of typhus patients from the area, VAN ROOYEN found that the rickettsia-agglutination reaction was of the epidemic type in 75 and of the murine type in 6.

A "Precipitin Colloid Test (Platinum Chloride)" devised by Major L. E. ELKERTON I.M.S. was tried. The antigen used was a mixture of four volumes of supernatant fluid taken from a rickettsia vaccine after standing for "some time" and three volumes of a 0.684 per cent. solution of platinum chloride. To 18 drops of distilled water (pH 6.6) one drop of serum is added after shaking one drop of antigen is added the mixture is shaken and 18 more drops of distilled water are added. Readings of the turbidity are then made. Positive reactions are said to occur earlier than with the Weil-Felix test, and are regarded as indicating the presence of antibodies of the specific infecting agent rather than the *Proteus* agglutinins.

Numerous guinea-pigs were inoculated intraperitoneally with the blood of patients. With the usual suspensions of macerated blood clot, typhus was transmitted from 8 of 31 cases but better results were obtained by centrifuging 20 ml. of blood mixed with 4 ml. of sterile citrate solution and using 2 ml. of the leucocyte and upper red-cell layer thus obtained as the inoculum. With this method five positive results were obtained in ten cases. Blood drawn in the first week gave the best results samples taken in the second week were slightly less suitable and third-week samples were seldom positive.

The febrile reaction in guinea-pigs was better shown when the intra-abdominal temperature was taken instead of the rectal temperature.

The morbid anatomy of the infected guinea-pigs is described in detail. VAN ROOYEN who examined 31 of the infected guinea-pigs found that the Iran-Iraq strains of epidemic typhus rickettsiae differed from the Egyptian in being more virulent causing (1) a tunica reaction (though this did not amount to a true scrotal reaction) (2) petechial haemorrhages into the peritoneum and (3) in many cases nodule formation in the brain such as was never seen among 200 guinea-pigs infected with the Egyptian strains. JOHN W. D. MCGEE

VIOLLE, H. & CALAMIT L. Sur une épidémie de typhus survenue à Marseille au camp d'hospitalisation des prisonniers allemands. [An Epidemic of Typhus in a Hospital Camp for German Prisoners in Marseilles.] *Bull Acad Mèd* 1948 v 130 Nos. 12, 13 & 14 229-31

LEVADITI J. C. & PANTHIER, R. La microscopie en fluorescence de *Rickettsia prowazekii* [Fluorescence Microscopy of *Rickettsia prowazekii*] *C. R. Soc Biol* 1945 Oct. v 139 Nos 19/20 890-92. [Refs in footnotes.]

*Rickettsia prowazekii* obtained from the lungs of infected rabbits were examined microscopically by ultra violet illumination. They were found to possess no natural fluorescence and although they could be made visible by staining with electro-positive fluorescent dyes they appeared identical in size and form with the organisms stained by ordinary dyes and examined with white light. Fluorescence microscopy therefore does not reveal any structural details such as have been observed with the electron microscope.

John W D Megaw

LEÓN A. P. Reacción de Weil Félix tipo Kahn. [The Kahn-Type of Weil-Felix Reaction] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Sept. v 6 No 3 173-9 English summary

The test described appears to be a rapid modification of the Weil Felix test. The apparatus employed is the same as that used in the Kahn test for syphilis and the procedure is on similar lines except that the antigen consists of a highly concentrated and standardized suspension of *Proteus OX19* and that 0.1 cc. of the serum to be tested is used instead of 0.15 cc.

The reading is made within 10 minutes the tubes are kept in the rack, and neither a lens nor a concave mirror is used.

The degree of agglutination in each of the three tubes is recorded as +, ++, +++ and ++++. When a total of 8-12 crosses is recorded in the three tubes the reaction is regarded as positive when the total is 2-7 crosses it is doubtful and with less than two crosses it is negative.

In a series of 33 tests of typhus sera in which the Weil-Felix titre ranged from 1-160 to 1-10 240 the reaction was positive in 30 it was doubtful in three in each of which the titre was 1-160.

In a group of 18 cases of typhoid fever there were no positive but 11 doubtful reactions in this group the Weil Felix titres ranged from 1-20 to 1-160.

Among 828 sera sent for the diagnosis of syphilis 466 gave doubtful and 11 gave positive responses among the same sera 628 gave Weil Felix titres ranging from 1-20 to 1-160 and two gave titres of 1-320 and 1-640 respectively. The 11 sera that gave positive reactions with the author's test reacted at titres of 1-80 to 1-640 with the Weil Felix test.

John W D Megaw

LEÓN A. P. & CANO Carmen. La reacción de fijación del complemento inversa en el diagnóstico del tifo exantemático [The "Inverse Complement-Fixation Test" in the Diagnosis of Typhus Fever] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Sept., v 6 No 3 167-72 English summary

The authors have confirmed the findings of SMORODINTZEF and DROBYSHEVSKAYA, who showed that the presence of a specific antigen could be demonstrated during the first few days in many cases of typhus fever [this *Bulletin* 1944 v 41 1021].

In the present experiments the complement fixation test was carried out by using known antibodies instead of known antigens. The antibodies were obtained by immunizing rabbits with intravenous injections of *Rickettsia prowazekii* var *mooseri* or of *Proteus OX19*.

All of nine typhus patients whose sera were tested before the 10th day of the illness gave strongly positive reactions. The average titre of two of these tested before the 5th day was 1-3 000 the other seven were tested between the 5th and 10th day and the average titre was 1-800.

Among 13 patients tested after the 10th day only four reacted the average titre was 1-300. In all of four convalescent typhus patients and in 13 typhoid patients the reaction was completely negative.

The reaction, therefore appears to be specially useful in the early stages of typhus attacks while the free antigens are still dominant and the standard complement fixation test based on the presence of antibodies, is still negative in most cases.

John W D Magee

D'IGNAZIO C. & CODELEONCINI E. Dermotifo in vaccinati. Nota clinica. [Typhus Exanthematics in Vaccinated Persons. A Clinical Note.] *Boll. Soc Ital di Med e Igiene Trop* (Sex Eritrea.) 1945 v 5 No 4 7-21

Evidence is produced to show that the original Weigl-type vaccine and a locally produced vaccine have had a striking effect in lessening the severity of attacks of typhus fever among European patients in Addis Ababa during the years 1938-41.

There were 55 cases of which four were fatal, among vaccinated persons. One of the patients who died was attacked before the end of his course of vaccination, and the other three had not been revaccinated during the previous three years. The case-fatality rate among unvaccinated patients was about 21 per cent.

John W D Magee

IMBROSCHI G. Sul valore teorico e pratico delle intradermoreazioni con i polisaccaridi del *Proteus X19* e della *Rickettsia prowazeki* per la diagnosi di dermotifo. [The Theoretical and Practical Value of the Intradermal Reaction with the Polysaccharides of *Proteus X19* and of *Rickettsia prowazeki* in the Diagnosis of Exanthematic Typhus Fever] *Giorn di Batteriol e Immunol.* 1945 Oct.-Dec. v 33 Noe 10/12 193-216 [11 refs.] English summary

The author has isolated the polysaccharide of *Proteus X19* by the method of ZIMMER and PARKER and, using CASTAGNEDA's technique he has obtained from this two fractions—the OA and OP factors. Both fractions together and separately were used in carrying out the intradermal tests. Rickettsial polysaccharides were also prepared from the intestines of infected lice by Castagneda's method. All the above substances were used in dilutions of 1-100 000 and 1-640 000. A filtrate of *Proteus* cultures was also employed in dilutions of 1-100 and 1-200.

The responses to intradermal injections of all these preparations were essentially similar—inflammatory reactions in healthy persons and in patients suffering from diseases other than typhus also in persons vaccinated with Weigl's vaccine—negative results in typhus patients from the 5th or 6th day onwards—and variable responses in typhus convalescents.

The test is regarded as specific and therefore of diagnostic value. A significant response is said to have been obtained in some cases before the Weil-Felix reaction became positive. False positives were observed in some cases when the *Proteus* filtrate was used—these were regarded as being due to sensitiveness of the patients to non-specific proteins contained in the culture medium.

Details of the methods employed and of the responses obtained in a large number of cases are contained in the paper.

John W D Magee

MILLER, E. S. & BEKSON, P. B. Murine Typhus Fever. *Medicine* 1946 Feb. v 25 No. 1 1-15. [30 refs.]

This description of murine typhus fever is based on a study of 126 cases seen at Atlanta, Georgia, during the eight years ending 1943. The diagnosis was based

on the observation of a clinical picture consistent with typhus fever together with a positive Weil Felix reaction at a titre of 1-160 or over. Some cases in which the Weil Felix reaction was positive were excluded because of the presence of a *Proteus* infection and there were other cases including three fatal, in which the clinical picture suggested murine typhus but in which the diagnosis could not be confirmed by a positive Weil Felix test.

Contrary to the usual belief the disease was as common among negroes as among white men. The month by month incidence, starting from January was—3 2 0 0 2 3 11 19 32 30 17 7.

There was a definite history of association with rats in 54 per cent of the cases but only two patients could recollect having been bitten by fleas so that the authors doubt whether infection is conveyed solely through actual contact with fleas. Contact with faeces of the insects or with urine of infected rats must be considered as possibilities.

The clinical features are described. They correspond to those of louse borne typhus of a mild type. A rash was seen in 80 per cent of the white and in 43 per cent of the negro patients. The percentage distribution of the rash was trunk 98 upper limbs 75 lower limbs 59 palms 14 soles 10 and face 10.

The only patient who died was a negro woman aged 60 who had uraemia on admission. There may have been three other fatal cases during the period among patients with unconfirmed diagnosis.

John W D Megaw

PHILIP C. B. WOODWARD T. E. & SULLIVAN R. R. Tsutsugamushi Disease (Scrub or Mite-borne Typhus) in the Philippine Islands during American Re-Occupation in 1944-45. *Amer J Trop Med* 1946 Mar v 26 No 2 229-42 1 fig [11 refs]

The authors state that it is remarkable that incontrovertible evidence of tsutsugamushi disease in the Philippine Archipelago was not forthcoming until its occupation in troops during the present war. They think it likely that cases described by ASHBURN and CRAIG in 1908 [see this *Bulletin* 1944 v 41 437], and other cases reported by FOSTER in 1912 under the name endemic typhus may have been instances of tsutsugamushi disease.

The present paper deals with the disease as observed during the reoccupation in 1944-45.

Altogether 222 cases of which 10 were fatal have been recorded from the following islands—Mindoro 95 Samar 88 Luzon 28 Negros 7 Leyte 3 and Mindanao 1. An eschar was seen in 40.5 per cent of the patients and a rash in 21.2 per cent. These figures are thought to be under-estimates.

Most of the cases in Luzon were closely investigated. In 15 of them samples of sera were tested by the complement fixation test by Dr Ida BENGTSOV [whose name as often happens is wrongly spelled as Bengston]. The reaction was positive in every case. The titre ranged between 1-64 and 1-32 768 in 14 cases.

The authors isolated a virulent strain of *Rickettsia orientalis* from a patient in Samar Island. This strain was subjected to stringent tests.

The infected localities were usually grass-covered land or neglected and scrub-infested coconut groves. *Trombicula deliensis* (syn. *T. walchi*) was found on rats in all the Islands in which the disease occurred except Leyte Island. *T. akamushi* (syn. *T. fletcheri*) was found in Luzon and Negros. The most important of the mite hosts appeared to be *Rattus mindanensis*.

John W D Megaw

Sera of 68 dogs from the same and other localities were then examined by the complement fixation test—titres of 1-256 or over were observed in 11 animals of which eight belonged to families in which cases of Rocky Mountain spotted fever were said to have occurred. Among 41 of the dogs that lived in localities in which Rocky Mountain fever was not known to occur there was only one positive reaction at a titre of 1-128, and no other at a titre above 1-16. For technical reasons the reaction at 1-128 was not regarded as being significant.

Some of the human patients gave no history of having been bitten by ticks, but were known to have pecked ticks from their dogs.

The authors state that the findings suggest more than a casual association between the dog and human cases but that further studies will be needed to elucidate the rôle of the dog in the epidemiology of the disease. They also point out that the dog has been implicated as the reservoir of the tick-borne boutonneuse fever and that Rocky Mountain fever has been transmitted experimentally to dogs by the bites of infected ticks [this Bulletin 1933, v 30 888].

John W. D. Mingo

## YELLOW FEVER.

GARNHAM, P. C. L., HARPER, J. O. & HIGSTON, R. B. The Mosquitoes of the Kaimosi Forest, Kenya Colony with special reference to Yellow Fever. *Bull. Entom. Res.* 1946, Feb. v 36 Pt 4 473-66, 3 text figs. & 6 figs on 2 pls. [21 refs.]

Two cases of yellow fever have occurred in Kenya in recent years, one at Kitale (1942) and the other at Kisumu (1943). To ascertain if Kenya forests are infected or if conditions in them are suitable for the development of the disease, investigations were started in November 1942, and continued until October 1944.

The Kaimosi forest lies north of the equator between Kisumu and Kitale. It is a semitropical rain forest covering some 50 square miles—the locality, vegetation, inhabitants and climate are first described and then a more detailed account is given of the mosquitoes of the area.

Adult mosquitoes were collected at ground level and on a fixed platform 55 ft. up a tree in the depth of the forest—they were also taken on a movable platform at different levels. Animal-baited traps attracted nothing, and collecting in huts yielded only small numbers. Larvae were taken at different heights from rot-holes in trees from axils of plants from bamboo and wooden containers hung in trees from bamboo sections placed on the fixed platform in the tree top and from many other places. The authors propose the term *acrodendrophily* to indicate the preference shown by certain mosquitoes for haunting tree tops.

The routine collections produced 55 species of ten genera, of which the following are some examples. *Culex nebulosus* was found at most levels even as high as 60 ft. The commonest larva in tree holes was that of *Aedes capensis* though adults were rare. *Aedes spicargenteus* was the commonest adult—it bites man readily and prefers light forest—larvae were not found in the routine collecting area but were taken from holes in fallen trees in the northern part of the forest. In the denser untouched forest *Aedes frazeri* larvae were found at all levels adults occurring in ground and tree top catches in the ratio of 3:5. Larvae of *Aedes longipalpis* were usually absent from ground-level collections, they and the adults were commoner in the tree-tops. *Aedes aegypti* a low-level breeder was never taken in huts but was frequently found

a mile or more inside the forest away from human dwellings. *Aedes africanus*, a known vector of yellow fever was commonest from August to November. It was found breeding in the buttress roots of trees and in containers up to 50 ft from the ground. Adults were taken mostly in the tree tops.

It seems that the selection of a breeding place depends more on height, shade shape and size than on the chemical composition of the water in it. Analysis of such waters showed that a breeding place of *Theobaldia fraseri* contained 79 parts of oxidizable matter per 100 000 [in Table VI a confusing misprint shows this mosquito as *A. fraseri*].

From the evidence accumulated during this survey it is concluded that conditions in the Kaimosi forest are adequate for the establishment of yellow fever. Some control measures are suggested.

H S Leeson

### DENGUE AND ALLIED FEVERS

WEYRAUCH H M & GASS H. Urogenital Complications of Dengue Fever. *J Urology* 1946 Jan. v 55 No. 1 90-93

Among 141 U.S.A. males who suffered from dengue in the South Pacific area in 1943-44 five had dengue orchitis as a complication or sequela of the disease. In one case the right testis became swollen and painful in the second month of convalescence and atrophy was observed six months after the attack. In the other cases orchitis occurred during the febrile stage. In one case the orchitis was unilateral and there was no atrophy in the other three the condition was bilateral it was followed in one case by bilateral atrophy in another by unilateral atrophy, and in the third there was no atrophy.

Five patients including two who had orchitis had bloody seminal emissions for one to four months after defervescence. The source of the haemorrhage could not be ascertained.

John W D Morgan

FLORIO L, HAMMON W McD, LAURENT Angela & STEWART Mabel O. Colorado Tick Fever and Dengue. An Experimental Immunological and Clinical Comparison. *J Exper Med* 1946 Apr 1 v 83 No 4 295-301 4 figs.

Six neuro-syphilitic patients were inoculated with strains of dengue virus obtained from the Pacific area, and in each case a typical attack of the disease was produced. Two of the patients were later re-inoculated with the virus and both were found to be immune. The other four were inoculated 40-80 days later with a strain of virus of Colorado tick fever which had been serially passaged six times through hamsters and then through two human volunteers. Typical attacks of Colorado tick fever were produced in three of the patients; the fourth had no definite reaction but he was known to have spent several years in areas where the disease is endemic.

Another patient was inoculated first with the virus of Colorado tick fever and 69 days later with the virus of dengue. Typical attacks of each disease resulted.

It appeared therefore that there was no cross immunity between the two diseases in spite of their striking clinical and haematological similarity and the approximate equality in the particle-size of their causative viruses.

The other chief difference between the diseases are stated to be the absence of rash in Colorado tick fever the non-transmissibility of dengue through hamsters and the natural transmission of the diseases by different vectors.

[Colorado tick fever appears to be primarily a disease of lower animals, transmitted from them to man by a tick if, as seems possible, it should come to be regarded as belonging to the same disease group as dengue it would be classed as a tick-borne, zootic, member of the group]

The charts illustrating the paper show that there is a remarkable resemblance between the fever curves and haematological findings of dengue and Colorado tick fever. The average duration of the latter fever is slightly longer the rise and fall of the temperature are somewhat less abrupt and no macular or maculo-papular rash occurs. A diffuse erythema was observed in all the dengue patients, but in two only of the four tick fever patients.

References to earlier work on Colorado tick fever will be found in this *Bulletin* 1941 v 38 664 and 1945 v 42, 117 and 118.]

John W. D. Meyer

POLLARD M. LIVESAY H. R. WILSON D. J. & WOODLAND J. C. Experimental Studies with Bullis Fever *Amer J Trop Med* 1946 Mar v 26 No. 2 175-87 7 charts. [11 refs.]

Two of the authors, LIVESAY and POLLARD have already produced evidence which they regarded as pointing to the probability that the disease was caused by a rickettsia [see this *Bulletin* 1944 v 41 209] and soon afterwards AMIGSTED and BADER reported the isolation of an organism which they believed to be a rickettsia [*ibid* 668]

After the investigation described in the present paper the authors conclude that "it would be premature to make any definitive classification of the agent without additional studies and that the agent "appears to approximate in size the elementary body agents such as ornithons more than it does the typical rickettsiae.

In four cases, the infection was transmitted to human volunteers by subcutaneous injection of serum or blood of infected persons. In one of these cases the serum of a naturally-infected patient was used after passage through a Seitz E.K. filter pad but the pad was not afterwards tested for accuracy serum from this experimentally-infected volunteer was found infective to another volunteer after passage through a Seitz E.K. pad which apparently was tested and found accurate. In the other two cases whole blood of naturally infected patients was employed.

After two preliminary passages through white mice a strain was passed serially through the yolk sacs of 5 or 6-day-old chick embryos, and small cocco-bacillary bodies were found in smears of the sacs, but not inside the cells. [In the previous report of Livesay and Pollard similar bodies were described as occurring inside the cells in peritoneal scrapings from infected guinea pigs, and in biopsy smears from lymph nodes of patients.] With yolk sac material of the 6th to the 20th passage, four volunteers were successfully inoculated.

Three experimentally-infected volunteers were later challenged with blood of patients suffering from Colorado tick fever and all responded with typical attacks so also did a person convalescent from naturally-acquired Bullis fever when challenged with a hamster strain of Colorado tick fever. It was concluded that there was no immunological relationship between the two diseases.

A strain of infection was obtained from a pooled suspension of the bodies of 337 *Amblyomma americanum* ticks collected from a deer in the area. This strain, after passage through mice and embryo chicks infected two volunteers who were later found immune to a strain of human origin.

The febrile responses in the experimental cases in human beings were usually slight in four of the temperature charts two or three fleeting rises to about

99°F are shown. In all the cases there were relative leucopenia headache body aches and lymphadenopathy

[The authors refer to the reviewer's suggestion that Bulis fever might be related to Colorado tick fever (see this *Bulletin* 1944 v 41 34 and 1945 v 42, 375) and although the present observations go to show that there is no immunological relationship between the two diseases they tend to support the speculative view that both fevers may be caused by filter passing viruses related to the virus of dengue. Final judgment on the exact nature of the infecting agent of this elusive disease must be suspended.] •

John W D Megaw

LAIGRET J & CORCOS A. Observation à Tunis d'une maladie épidémique se manifestant par de la fièvre et des vomissements de sang. [Observations on an Epidemic Febrile Disease with Haematemesis, in Tunis.] *Bull Acad Méd* 1946 v 130 Nos 3 4 & 5 55-7

Between mid September and Mid November 1945 the authors saw eight cases of a short, acute fever lasting three to five days and ending with haematemesis. Other cases have been seen by their fellow practitioners in Tunis

The onset and early stages of the illness conformed to the clinical pattern often seen in dengue and sandfly fever except that a feeling of painful heaviness in the epigastric region and nausea were the most prominent symptoms. About the third day the patients suddenly vomited considerable quantities—up to 300 cc.—of red or black blood. Immediate relief followed and the temperature began to fall, reaching normal within about two days. There were two deaths one in the case of a child aged two years. Although *Aedes aegypti* were abundant it was possible to exclude yellow fever because of the immediate relief following the haematemesis. Bacteriological investigations yielded negative results. The disease was regarded as a severe form of the pseudo dengue which had been prevalent in Tunis since the spring of the same year. There had been hundreds of cases of this fever which differed from dengue in the complete absence of a rash. Sandfly fever also was ruled out because neither relapses nor recurrences of the fever were observed. It was concluded that the fever was like dengue or three-days fever but was neither the one nor the other and that a suitable name would be Tunisian gastroenteric fever

[The line of reasoning of the authors is not easy to follow. They regard the fever as a severe form of pseudo-dengue yet they suggest a name that is obviously unsuitable for a disease of that type. Their only stated reason for excluding sandfly fever—the absence of relapses—is surprising. Altogether the evidence supplied seems compatible with the view that haematemesis may have occurred as an exceptional complication in eight out of several hundred cases of a fever of the dengue group.]

John W D Megaw

## PLAGUE.

BULL. U.S. ARMY MED DEPT 1945 Apr No 87 13-18 Plague in Dakar

An outbreak of 567 cases of plague occurred in Dakar "the largest city in French West Africa" in 1944 during the period April to November with a 91 per cent. mortality. No cases of plague had been recorded there since 1937 and so this was essentially a war time epidemic. Most of the interest of this account centres upon the dusting technique and control of the native population. All the actual cases of plague were "in native blacks except one in a Syrian and



three in French Europeans." American help was enlisted for the anti-plague dusting programme although this was vigorously entered on only after "the seasonal decline of the plague incidence had begun." A division of the native section of the town was made into zones controllable by a cordon of 200 to 300 gendarmes. Each zone was selected the night before operational treatment to prevent exodus and four or five "outlet stations" were established. Dusting was commenced at about 6 a.m. and was carried out by three or four native workers using 10 per cent. DDT dust with Hudson plunger type dusters. The treatment began at the ankles dusting under the various layers of clothing then dusting at the waist—front and rear then at the sleeves and neck and finally the hair. The clothing was held out and down to form an envelope for the dust which could be seen through the fabric as it was applied on the inside. The operation, to allow of release of the outgoing working native population was complete in about an hour and then the cordon arrangements were modified to deal with the remaining population. It is reckoned that less than 5 per cent. of the people were not dusted. Further anti-flea measures consisted in treatment of the houses "by dusting with 10 per cent. dust and by spraying with 5 per cent. solution in kerosene" where attention was specially directed to the floor and lower walls and beds which were heavily infested with bed bugs as well as fleas. "All public houses such as cafes restaurants bars, brothels cinemas etc. were sprayed with 5 per cent. DDT solution." A survey showed that of 316 houses infested before spraying all but 7 were completely free of fleas two weeks after treatment. The rat population in this area was very large and comprised, more or less equally the Norwegian, Alexandrian and the common rat. The Camtcheonli rat was not so numerous. Poisoning of the rats was barred because of danger to children and domestic animals. French opinion was that the best results in plague treatment was obtained by combined sulphadiazine bacteriophage therapy

W F Harvey

KARTMAN L. A Note on the Problem of Plague in Dakar Senegal, French West Africa. *J Parasitology* 1948 Feb. v 32 No. 1 30-35 2 figs. ✓

Dakar experienced an epidemic of plague in 1944 and is regarded as an endemic focus. The present communication insists on the possibility of a human flea being a main plague vector in some regions—in Dakar for example, where the rat flea *Xenopsylla cheopis* although the commonest species on rats is quite negligible in native huts of the villages about Dakar. Identification of the various species of fleas collected was carried out at the British Museum and showed that the house and body flea in the Dakar area was *Synosternus pallidus*. The genus *Synosternus* is closely related to *Xenopsylla* and the species *S. pallidus* is parasitic on rodents the hedgehog and various carnivora. A very instructive table gives percentages of various fleas collected for examination —

Species	From rodents	From floors
	Per cent.	Per cent.
<i>Xenopsylla cheopis</i>	75.95	1.10
<i>Echinophaga gallinacea</i>	12.83	18.40
<i>Ceratophyllus felis</i>	4.45	0.35
<i>Synosternus pallidus</i>	6.75	80.15

This shows the complete reversal of percentages for *X. cheopis* and *S. pallidus* according as the collection was made from rodent or from the floors of native huts. "It is suggested that further study of *S. pallidus* as a potential vector of plague in the Dakar area is indicated."

W F Harvey

LAHNUM W. H. Mammals and Plague Distribution in the United States. *U.S. Army Med Bull* 1946 May v 46 No 5 782-5

This contains a useful list of mammals that have been found to be infected or to possess ectoparasites infected with plague

HORNIBROOK J W Streptomycin in Experimental Plague *Pub Health Rep* Wash. 1946 Apr 12 v 61 No 15 535-8

Reports are now appearing which deal with the therapeutic possibilities of streptomycin—from *Actinomyces griseus*—in human diseases especially those due to Gram negative bacteria. Its toxicity for animals is low and it is more active than streptothrycin. This condensed article which is full of detail gives an account of experiments on plague in mice

The material used contained approximately 200 000 units per gramme killed a 14-gm. mouse on intraperitoneal injection of 20 mgm as 5 per cent solution and failed to kill a 15-gm mouse receiving 10 mgm. In the therapeutic tests treatment was started 3 and 2 days respectively following inoculation with live organisms. If visible swelling at the site of inoculation did not occur the mouse was regarded as non infected and, together with those that died, was excluded from the testing trials. At the end of 14 days from the time of inoculation all surviving animals were killed, autopsied, and the spleens cultured and those mice dying within the 14 days after inoculation of a dose of living plague up to 6 000 organisms in the group were considered to have died of plague. A control series one with no treatment and one with sulphadiazine in the same dosage as streptomycin except for the first dose which was 5 mg rather than 2 mg was set up and this series (Table 5) is summarized. The summary of the entire experiments is as follows—

Streptomycin is thermostable. It is inhibitory to *P. pestis* in broth in a dilution of approximately 1/160 000. When 2 mg (400 units) were given before and 2 mg 24 hours after challenge 10 mice survived for 14 days a dose of plague organisms which killed 70 percent. of the controls. When treatment (2 mg per day) was started 2 days following inoculation and continued for 6 days 9 of 10 mice survived for 14 days. When sulfadiazine was used under the same circumstances 4 of 11 survived 8 of 9 controls died. (Table 5)

W F Harvey

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## CHOLERA

MARKOWITZ J Experiences with Cholera in a Jungle Camp in Thailand. *J Roy Army Med Corps* 1946 Apr v 86 No 4 150-53 2 figs

[This is one of a remarkable series of articles written in this number by two prisoners of war in Japanese hands. Undoubtedly the entire series should be given wide publicity for their pictorial and textual illustration of sheer devilish, human cruelty and incidentally as testimony to the self-sacrifice and medical ability of the Royal Army Medical Corps under what may euphemistically be described as adverse conditions. The tales far exceed in their general interest the information relating to particular diseases.]

Much the same type of restricted epidemic, if not identical has been summarized below. This epidemic relates to a community of 7 000 more or less disabled British and Dutch prisoners of war. A final table is a Diary of Events and shows that of 134 cases admitted as true cholera 53 were fatal. One concluding remark may be transcribed—Anuria resulting in uraemia was an uncommon cause of death. In brief a patient could die from cholera either from loss of fluid so that his plasma oozed out through the bowels—a

condition comparable to high intestinal obstruction or to shock displayed in a patient grossly scalded by steam or he could die of toxæmia as in any other infectious disease. The actual conclusion to the article stresses certain special points in treatment—distilled water if taken fresh from the still is not pyrogenic and can safely be used. Some advantage is claimed for intravenous infusion with 2 per cent. salt solution over 0.85 per cent. (normal) salt solution. "One litre of distilled water hot off the still is treated with 50 c.c. of 25 p.c. sodium chloride stock solution. The latter need not be fresh.

W F Harvey

DE WARDENER H. E. Cholera Epidemic among Prisoners of War in Siam. *Lancet* 1946 May 4 637-40 1 chart.

The account of this cholera epidemic presents the reader with another shocking tale of Japanese barbarism and cruelty to defenceless prisoners of war. It brings into prominence the notorious instance of the construction of the Siam-Burma railway. Some very interesting facts emerge from the details given of what was to a very large extent an untreated epidemic under the worst possible sanitary conditions. It lasted apparently in acute form for about 5 weeks and seems to have subsided spontaneously. Total figures of cases at risk were 200 British officers and 1 400 British other ranks. 173 cholera cases were admitted and the deaths among these admissions to so-called hospital numbered 100 (57.8 per cent.). A Dutch camp of 250 sick persons afforded a control series. In this there was only one case of cholera (with recovery) at the same time and under more or less similar conditions to the British. The immunity of the Dutch was not confined to this area but was observed in all the camps on the river. As an explanation of what was a very real difference the suggestion is made that recent vaccination (4 weeks previously) and regularly yearly inoculations protected the Dutch and gave them immunity.

Common complications and sequelae are listed as (1) coma (2) gangrene (3) multiple abscesses (4) severe anorexia leading to quick onset of deficiency disease and (5) residual diarrhoea. These same complications however seem themselves to have been to some extent complicated by the originally sick state of the population at risk, with chronic malaria dysentery beriberi, hyporiboflavinosis and pellagra. As is common in such epidemics the first cases were not recognised. Facilities for treatment were totally lacking and the difficulty was increased by the onset of the monsoon.

W F Harvey

BLASS Judith. Etude de la consommation du glucose par les vibrions cholériques non proliférants [The Consumption of Glucose by "Non-Proliferating" Cholera Vibrios.] *Ann. Inst. Pasteur* 1946 Mar-Apr v 72, Nos. 3/4 230-40 4 figs.

A new method of preparing cholera toxin was devised by BERNARD and GALLUT [this *Bulletin* 1945 v 42, 34 807] and the present work is designed to study in detail the utilization of glucose in the process. Experimental work is straightforward to determine (1) the maximum quantity of glucose consumed by a fixed concentration of vibrios where the variable is the glucose content of the medium (2) the consumption of glucose per unit of time with fixed glucose concentration (5/1 000) (3) the consumption of glucose as a function of the medium (4) the products of fermentation of glucose by the non-proliferating vibrios in Ramon bouillon. Products of fermentation were lactic acid, succinic acid, formic acid ethyl alcohol and traces of aldehydes which are the same as those of vibrios grown in synthetic glucose media. The maximum

quantity of glucose utilized was 4 to 5 gm per litre whatever the concentration of the vibrios and consumption was accompanied by a fall of pH from 8 to 5.8 which was fatal to the vibrios. Increase of concentration of the vibrios produces a more rapid fall in the pH. An important factor which determines the utilization of the glucose is the buffering power of the medium.

W F Harvey

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## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

LAMY L. Action du para-aminophénylsulfamide (1162 F) sur le départ des cultures d'entamoebadysenteriae (Deuxième note) [The Action of Sulphanilamide on the Starting of Cultures of *Entamoeba histolytica*] *Ann Inst Pasteur* 1946 Mar-Apr v 72, Nos 3/4 295-7

In a previous paper [this *Bulletin* 1946 v 43 442] the author showed that the presence of sulphanilamide [1162F] was favourable to the development of *Entamoeba histolytica* in cultures in the present paper he records experiments which show that in concentrations of 1 1 000 1 500 and 1 200 it favours the development of the amoebae from cysts in faeces sown on the medium without any preliminary treatment.

Cultures of active amoebae were obtained by the 4th day in all three concentrations of sulphanilamide but the amoebae were much fewer in that of 1 200 than in that of 1 1 000. The first subculture made after 7 days was positive and the original culture still showed living amoebae after 10 days the medium was the same as that previously used. The addition of rice starch supplied a nutritive factor to the amoebae and also hinders the growth of *Blastocystis* which is further hindered by the sulphanilamide as are also bacteria.

The author also refers to abstracts to this *Bulletin* of papers by CHIRY *et al* [1942 v 39 785] and by RODANICHEZ and KIRSNER [1943 v 40 455]

J F Corson

TSUCHIYA, H & KENAMORE B. Report on a Case of Balantidiasis. *Amer J Trop Med* 1945 Nov v 25 No 6 513-14

The case reported was in a woman 35 years of age who had suffered from persistent diarrhoea associated with abdominal pain of four months duration. There was no history of contact with pigs. The condition was cured by carbarsone treatment.

C M Wenyon

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## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

PAVLOVSKY E N [On the Natural Focal Distribution of the Tick Relapsing Fever in the Turkoman Soviet Socialist Republic.] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 3 56-9 1 fig [in Russian.]

The author notes that within the territory of the Turkmenistan the vectors of tick borne relapsing fever are represented by three species of *Ornithodoros*. The most important and widely distributed of these is *O papillipes* the second is *O nereensis* a new species described by the author which lives in burrows and under stones but does not occur in human dwellings while the third *O tartakowskyi* was found in the burrows of rodents. These ticks are occasionally found to be spontaneously infected with spirochaetes of gerbils (*Rhombomys*

[August, 1946]

*opimus*) in the valley of the river Murgab. To distinguish this spirochaete from the causative organism of human relapsing fever in Middle Asia (*Spirochaeta sodanum*) it was named *S. letyschovi*.

In spite of the presence of these three vectors tick-borne relapsing fever occurs in Turkmenistan only in rare sporadic cases whereas it is much more common in Uzbekistan and in Tadzhikistan. This is due to the fact that *O papillipes* is a rare species in Turkmenistan while *O. nersensis* and *O. letyschovi* inhabit biotypes with which man does not as a rule come in contact.

The author describes the case of two men who had taken shelter in a cave near Ashkhabad and who developed relapsing fever nine days later after showing typical traces of tick bites on the skin. An examination of the cave revealed ticks *O. papillipes* with a natural infection of spirochaetes. These facts point to the cave as a natural focus of tick-borne fever which is probably primarily a disease of lower animals (zoonosis) upon which the ticks feed.

C A Hoare

SOZIEV M S & LEONOVA N A. [New Data on the Reservoirs of the Virus of Tick borne Relapsing Fever in the Uzbek Soviet Socialist Republic.] *Moscow Parasit & Parasitic Dis.* Moscow 1945 v 14 No 3 60-65 1 fig [In Russian]

This paper is devoted to a study of the reservoir hosts of tick borne relapsing fever in Fergana (Uzbekistan). Previously the following animals have been found in Middle Asia to be naturally infected with spirochaetes of relapsing fever: dogs, rats (*Rattus turkestanicus*), gerbils (*Rhombomys opimus* and *Gerbillus evermanni*), bats (*Rhinolophus ferrumequinum*) and mice (*Apodemus musculus severinovi*). In Fergana the principal reservoir hosts were found to be mice 6 per cent. of which proved to be naturally infected. The duration of the disease in these rodents is 12-28 days and it is thought that in the course of the summer probably all the mice become infected. In view of their constant migrations it is suspected that mice serve as carriers of infected ticks (*Ornithodoros papillipes*) from house to house thus serving to disseminate relapsing fever. Experiments with spirochaetes obtained from mice proved that they were infectious with spirochaetes obtained from man.

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C A Hoare

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spirochaetes likewise failed to acquire an infection. It is concluded from these and previous experiments that *O. lahorensis* is not a vector of relapsing fever  
C A Hoare

TROITSKY N V [Transmission of the Tick borne Spirochaetosis by the various Stages of *Ornithodoros papillipes*] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 3 70-75 [In Russian.]

In the course of its metamorphosis the chief vector of tick borne relapsing fever in Middle Asia, *Ornithodoros papillipes* passes through one larval and from three to five nymphal stages. In each stage the ticks feed at least once on some vertebrate animal. From 20 to 50 or more days after feeding the tick moults and is transformed into the next stage of development. After moulting nymphs of the last stage become adult males or females which feed repeatedly but do not moult.

The author records the results of experiments carried out to determine the ability of different stages of the tick to transmit spirochaetosis. The ticks used in these experiments were collected from a disused and dilapidated piggery and repeated examination of random samples failed to reveal any natural infection among them. Guinea pigs were used both as the source of infection of ticks and to test the infection in the latter.

It was demonstrated that all the stages of development of *O. papillipes* from larva to sexually mature imago were capable of acquiring an infection by ingesting blood containing spirochaetes. They were all capable of retaining the spirochaetes in the successive stages of their development and of infecting susceptible animals by bite. Moreover it was shown that the spirochaetes can be transmitted hereditarily through the ova of the ticks which is an important epidemiological factor. After having fed on blood containing spirochaetes the ticks are capable of transmitting the infection by bite only after the expiration of a certain interval of time which varies with the stage of development. In sexually mature adults it is from one to two months while in larvae and nymphs the interval is determined by the time of ecdysis. Several days after the infective feed the number of spirochaetes in the body of the tick gradually diminishes until it becomes very small thenceforth remaining at a low level.  
C A Hoare

TROITSKY N V [Experiments on the Application of Carbon Disulphide, Chloropierine, K-Soap and other Insecticides for destroying and repelling the Ticks *Ornithodoros papillipes*] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 3 75-8 [In Russian.]

The author notes the importance of *Ornithodoros papillipes* as a vector of tick borne relapsing fever in Middle Asia, where up to 100 per cent. of the population in endemic areas are affected. The existing methods of destruction of the tick are unsatisfactory mainly owing to the inaccessibility of its habitats (cracks in the walls of houses, fine sand or dust in caves, etc.) and also because of the absorption of the insecticides by the substratum. In the present paper an account is given of the results of tests on the effect upon these ticks of various chemicals which were tested both for their lethal and repellent properties.

For lethal tests the ticks were placed in jars or in desiccators with a layer of sand or soil, into which they burrowed themselves. In the case of chloropierin about 100 cc. per cubic metre acting for five to six hours were required to kill the ticks. Paradichlorobenzene in a dosage of 250 cc. per cubic metre killed all the ticks only after 30 to 33 hours. The best results were obtained

with carbon disulphide which killed the ticks in a dosage of 250 cc. per cubic metre after exposure for 24 hours. It is concluded that the most practicable method for tick infested buildings is the successive treatment with two insecticides. First with carbon disulphide the fumes of which rapidly fill the room and can be eliminated after six to twelve hours and second with paradichlorobenzene which, when placed in suitable positions, prevents fresh infestation of the building.

As regards repellents, the following were tested — Paradichlorobenzene, "C.I." (naphthalene 84 parts, creosote and Iodoform, 3 parts each, which were made into a 5 to 10 per cent. solution in petrol) menthol, soap "K" and tar preparations. These were tested on guineapigs which were either powdered with the preparation or clothed in an overall soaked in a solution of the preparation. None of these tests gave completely satisfactory results.

C. A. Hoare

LEONOVA, N. A. [On the Possibility of Transmission by Lice of the Spirochaetes of Tick-borne Relapsing Fever *Sp. uzbekistanica* (= *Sp. sogdianum*) *Med. Parasit. & Parasitic Dis.* Moscow 1945 v 14 No 3 79-82. [In Russian.]

The author describes the results of experiments designed to test the viability of spirochaetes of the Middle Asia type of tick-borne relapsing fever in the body-lice, and the possibility of their transmission by this insect.

In two series of experiments, lice collected on human beings and bred in the laboratory respectively were allowed to feed on mental patients infected with *Spirochaeta uzbekistanica* for therapeutic purposes. The results were assessed (1) by emulsifying the lice and injecting the emulsion into guineapigs, and (2) by examining the intestinal contents of the lice under dark-field illumination and in stained smears. In a third series of experiments lice were inoculated by Weigl's method, with citrated blood of a guineapig containing numerous spirochaetes. The lice were subsequently dissected and their intestinal contents were examined microscopically under dark-field illumination.

In all of these experiments the results were consistently negative. It was demonstrated that the spirochaetes lose their viability several hours after inoculation into lice which are incapable of transmitting the infection to guineapigs.

C. A. Hoare

DESPORTES, C. & CAMPAÑA, Y. Sur *Ornithodoros tholozani* (Laboulbène et Mégnin 1892) et sur les ornithodores de l'Asie centrale et mineure. [O. tholozani and other Ticks of the same Genus in Central Asia and Asia Minor.] *Ann. Parasit. Humains et Comparés* 1946 v 21 Nos 1/2, 74-83 3 figs. [10 refs.]

ZARAFONETIS, C. J. D. INGRAHAM, H. S. & BERRY, J. F. Weil-Felix and Typhus Complement Fixation Tests in Relapsing Fever with special reference to *B. protensis* OX-K Agglutination. *J. Immunology* 1946 Mar v 52, No 3 189-99 1 chart [12 refs.]

Weil-Felix and typhus-complement fixation tests were carried out on sera of 50 patients under treatment for louse-borne relapsing fever in a Cairo hospital. The diagnosis was confirmed in every case by finding spirochaetes.

*Proteus* OXK was agglutinated usually in rising titre in every case. In 9 patients the maximum titre of complete agglutination that was observed was 1-40. In 11 it was 1-80 and in 30 it rose to 1-160 or over. Titres ranging from 1-640 to 1-2,560 were observed in as many as 14 of the patients.

Among 351 patients suffering from typhus, typhoid fever, smallpox, and

other diseases the positive reactions with OAK were —27 at 1-40 7 at 1-80 and 4 at 1-160

Among the relapsing fever patients there were two who reacted at high titres with the OY19-agglutination and the typhus-complement fixation tests and who presumably had typhus fever as well as relapsing fever apart from these only one relapsing fever patient reacted with either of these tests at a titre higher than 1-80 and in his case the typhus-complement fixation reaction remained constant at 1-160 on the 2nd 9th and 15th days

The author mentions the findings of ELSDON DEW who observed OAK titres of 1-100 or over in 211 of 650 patients suffering from louse-borne relapsing fever in Ethiopia [this *Bulletin* 1944 v 41 486]

From the table it appears that the maximum OAK titre in the authors relapsing fever patients was usually reached by the end of the second week, though in a few cases the titre continued to rise during the third week

John W D Megaw

MARTÍNEZ BÁEZ M. & VILLASANA A. Sobre la histopatología de la fiebre recurrente experimental. [The Histopathology of Experimental Relapsing Fever] *Rev Inst Salubridad y Enfermedades Trop* Mexico 1945 Sept. v 6 No 3 185-94 10 figs [14 refs.] English summary (2 lines)

The brains of 15 white rats infected by subcutaneous injection of *Spirochaeta noryi* were examined microscopically 8 were killed during the febrile attack and the other 7 at various times from a day to two months after the end of the attacks when no spirochaetes could be found in the blood.

In rats killed during the febrile attack there was intense congestion of the vessels of the pia mater and of the cerebral capillaries in 3 rats recent haemorrhagic foci 1-2 mm in diameter and of varying depth, were seen in the cortex and at the margins of these haemorrhages spirochaetes were very numerous Spirochaetes were found also in the cerebral capillaries the vessels of the pia mater the choroid plexuses and the parenchyma of the brain. An intense microglial reaction was always present especially in the cerebral and cerebellar cortex, and in the cornu ammonis. No changes were observed in the nerve cells and no reaction in the neuroglia.

In rats killed later no old haemorrhages were seen and it is suggested that they had been absorbed. No special pathological lesions were seen except discrete lymphocytic infiltrations in the pia mater

The paper is illustrated with ten photomicrographs

J F Corson

MUWAZI E. M. K. Penicillin in Treatment of Relapsing Fever *East African Med J* 1946 Feb v 23 No 2, 55-64

A record of the treatment of 37 cases of African tick fever (*Spirochaeta duttoni*) at the Mulago Hospital Uganda carried out in order to compare the therapeutic efficiency of penicillin and arsenicals

The patients were divided into three groups. Eleven patients were treated with sodium penicillin in doses ranging from 100 000 Oxford units in 24 hours to 900 000 units in 72 hours Five of them relapsed and one had seven relapses It is also of interest that several patients in this group were not without symptoms such as headaches and limb pains during the intermissions

Eight patients were used as control and treated with a single dose of 0.6-0.9 gm. of neocarsphenamine (N.A.B.) injected intravenously Five of them relapsed and two showed five relapses each

Eighteen patients were treated with total doses of from 100 000 to 900 000 units of penicillin in 24 to 72 hours combined with single maximum doses (0.75-0.9 gm.) of N.A.B. Seven relapsed and one patient had four relapses.



The author remarks that it is difficult to assess the therapeutic efficacy of penicillin since natural recovery occurs in a high percentage of cases of relapsing fever. Moreover the initial fever is not prolonged and the apyrexial intervals are of very irregular duration which, combined with the difficulty of controlling the patients made it almost impossible to follow up the cases adequately.

The results indicate however that neither penicillin nor N.A.B. either alone or in combination, is effective in preventing relapses in African tick fever. Both of them shorten febrile attacks but neither is an effective remedy which has yet to be discovered.

E Hindle

SCHUHARDT V T & HEMPHILL, Emmarie C. Brain Involvement as a possible Cause of Relapse after Treatment in Spirochetal Relapsing Fever. *Science* 1946 Apr 5 422-3.

A discussion of the results of experiments on the treatment of rats infected with a strain of relapsing fever transmitted by *Ornithodoros turicata* by means of penicillin sodium administered both intraperitoneally and intracranially [see this Bulletin 1945 v 42 735]

A total of 53 rats were infected with similar doses of blood containing spirochaetes and penicillin therapy was begun on the second or third day after their blood became positive. Twenty-five rats were each given 1 000 units of penicillin in a single intracranial injection and the 23 survivors received 1 to 14 intraperitoneal injections of penicillin at 3-hour intervals in doses ranging from 4 400 to 50,900 units per kgm. body weight. Nineteen rats were treated by intraperitoneal injections alone and nine were kept as untreated controls. All these nine were brain positive when tested 31 days later.

The total of 27 treated rats which received less than 40 000 units/kgm. all relapsed, regardless of whether they received intracranial injections or not. The relapse and positive brain infections of the 13 rats receiving intracranial injections are interpreted as the result of inadequate therapy to cure the infection in blood or visceral tissues. Fifteen rats received more than 40 000 units/kgm. and 10 of these intracranial penicillin. Of the latter 6 received only 4 injections and 3 showed positive brain infections possibly as the result of adhering infected blood the other 4 rats remained negative including brain passages, after 31 days.

The 5 rats receiving no intracranial injections all relapsed or showed positive brain infections.

The results support the view that after intraperitoneal treatment, relapses may occur as the result of spirochaetes re-entering the blood after persistence in the central nervous system.

E Hindle

Box, R. Het voorkomen van de rattebeetspiraal in de oorspeekselklier van de muis. [The Presence of *Spirillum minus* in the Ear Salivary Glands of Mice.] *Acta Leidensia (Scholas Med Tropicae)* 1940-41 v 15-16 143-51 [12 refs.] English summary

Many weeks after the infection the causative agent of rat-bite fever is found in larger numbers in the ear salivary glands of mice than in their blood. This speaks in favour of a possible rôle of the saliva in the transmission.

"The author has not succeeded in demonstrating the organisms in sections of salivary glands and other organs. So she doubts the exactness of the researches of KURAMA, KOBAYASHI, KARAI and others who might have taken perves for Spirilla."

NITTI F CONGE M & KAUFFMANN G Mlle Traitement du sodoku expérimental du cobaye par de faibles doses de pénicilline [The Treatment of Experimental Rat-Bite Fever in the Guinea-pig with Small Doses of Penicillin.] *Ann Inst Pasteur* 1946 Mar-Apr v 72 Nos 3/4 294-5

Few guinea-pigs were available and only small quantities of penicillin but four experiments were made with daily doses of 600 to 1 000 units per kgm in each experiment and in every guinea-pig treated, the spirilla disappeared from the blood and in some cases the animals ceased to lose weight. Relapses occurred after 4 to 30 days according to the dosage of penicillin given and the animals died. The authors think that at least a certain proportion of cures may be hoped for with the use of larger doses. [See also LOURIE & COLLIER this *Bulletin* 1944 v 41 293] J F Corson

## LEPROSY

CERRI B Ricerche sul sangue e sul midollo sternale nella lebbra. [Studies of the Blood and Sternal Marrow in Leprosy] *Haematologica* Pavia. 1942 v 24 Nos. 3 & 4 167-244 209-334 12 figs (2 coloured) & 6 graphs [47 refs.] French summary

Not all of this long article is taken up with the subject as stated in the title. For example, several pages are given to the history of sternal puncture and its uses in venereal and cutaneous diseases including syphilis and Kaposi's disease which have nothing to do with leprosy. On the other hand, the author includes other matters concerned with leprosy such as the results of biopsy of the skin and of examinations of the nasal mucus.

For his specific purpose the author took blood from the finger tip and marrow from the sternum, both in the morning of the same day and also material from the nasal mucus and from puncture of an inguinal lymphatic gland and, when the patient consented, of biopsy material from a leprotic lesion. For examination the methods of staining were the May-Grünwald-Giemsa and the Ziehl-Neelsen.

The patients comprised 23 with the nodular type of disease 11 with mixed leprosy and one with the nervous form. Details of each of the 35 are given, in letterpress and in tables the examinations were very full. Of the blood estimations were made of the haemoglobin the number of red and white cells and a differential count of 400-500 of the latter. The examinations of the marrow were much more exhaustive 20 varieties of cells were counted and their relative percentages calculated. [We have checked the first ten of these tables and in one instance only does the total come to 100 per cent. all the others exceed this ranging between 102.2 and 110.6 per cent. The percentages in the blood counts are more often correct.] Leucopenia of 2 600 and 4 150 respectively was found in two cases the one in the nodular group the other in the mixed leprosy group. Leucocytosis up to 14,850 per cmm. was found in five 2 of the first group (nodular cases) and 3 of the second (mixed). Another of the first group during a leprosy reaction, had a leucocytosis of 26,900 per cmm. Anaemia was a constant feature, nearly always hypochromic with some degree of anisocytosis and, rarely, poikilocytosis neutrophil metamyelocytes were also always present but not in large numbers non-segmented neutrophils were more common up to 35 per cent. of the neutrophils.

In the marrow points specially noted were asynchronism of maturation of cells asymmetry fusion of chromosomes pyknotic and staining irregularities. In general the marrow showed abundance of worn-out cells scarcity of areolar tissue and of vacuolated cells activity in production of granuloblasts raised leuco-erythroblast ratio and increased karyokinesis increase of myelocytes and metamyelocytes and predominance of erythropoietins over leucopoietins lymphocytes and monocytes showed a moderate increase eosinophiles generally below normal haemocytoblasts and histiocytes variable, but on the low side. In general the marrow presented signs of degeneration of cells and departure from the normal in size relative proportion of nucleus to protoplasm, of "over-granulation" with atypical forms and staining affinities, and atypical also in the number of nuclei in the granulocytes and polychromatophils with basophilic granulations in the erythrocytes.

In the material obtained by puncture of the inguinal glands the author noted cells of varied size sometimes "very large" (size not stated), with a histioid or monocyte nucleus the protoplasm basophilic with acidophilic particles, with clean-cut edges and vacuolated also typical plasma cells some binucleate and Türk's cells.

Biopsy specimens were obtained from five patients and from four material from scarification of lepromata there was nothing calling for special mention in these.

Examination for bacilli of leprosy in the marrow gland-junction skin and nasal mucus may be summarized as follows. They were found in all four situations in six of the patients and all were in the first group of nodular cases. In the marrow smears in 16 of the first group three of the second (mixed leprosy) not in the nerve-type patient. The last may be disposed of in a few words the skin was not examined but no bacteria were found in any of the other situations. As regards the gland-puncture results. In the 23 of the nodular group Hansen's bacteria were seen in 17 few in some, numerous in others sometimes singly sometimes in masses five were not examined by gland puncture and in one of those examined none was found. In the second group of 11 they were found in five and not found in three three were not examined. The skin was examined in nine of the first group only and infection was present in all. The nasal mucus was negative in three of the first group positive in the other 20 negative in two positive in none of the second group absent, as already stated, in the nerve case.

H. Harold Scott

SHLEMOVITZ, N. Leprosy—a Report of Nine Cases among Natives of the Mount Hagen Area in New Guinea. *Med. J. Australia*. 1946, Mar 16 v 1 No 11 369-70 4 figs.

This is an illustrated account of leprosy cases found in the mountainous interior of New Guinea at an elevation of 5,000 feet, where the disease had not previously been reported. It is however well known in the low coastal areas in which there was a leprosarium at Mandang. Some of the cases are of long standing and the disease therefore is not of recent importation. Three of the patients showed advanced neural signs with the development of claw hands three more were earlier neural cases with discoloured patches and alterations of sensation. Another showed thickened ulnar nerves without deformity of the hands but with a few ulcers about his ankles. The remaining two were lepromatous cases one showed large nodules containing numerous lepra bacilli, and the other involvement of the nose and larynx. Arrangements for isolation of these patients are being considered, and it is stated that leprosy undoubtedly exists in other localities in the interior of New Guinea.

L. Rogers.

ARNOLD H. L. Jr. Differentiation of Lepromatous from "Neural" Leprosy: The Basis, a Method, and Report of Five Cases. *Arch Dermal & Syph* 1945 Nov-Dec. v 52, No 5 354-64 7 figs. [Refs. in footnotes]

This is a useful and up-to-date paper by an experienced worker in Hawaii on the diagnosis of the types of leprosy as a basis for prognosis and preventive measures. The author deprecates the use of the term mixed leprosy in that it is not applied to a mixture of the main lepromatous and neural types but really means that the sites of involvement—both skin and nerves—by the lepromatous forms are mixed for in nearly every case of leprosy lesions of both the skin and the nerves are found. Lepromatous cases are characterized by the presence of raised red patches or diffuse granulomatous infiltration of the skin rich in *Mycobacterium leprae* and in advanced cases many of the internal organs are involved nerve trunks are also implicated with resulting paralyses and loss of sensation of the extremities. The eyes nose and larynx suffer severely in late cases and chronic nephritis and amyloid disease of the organs are important complications. The skin lesions can be differentiated from the tuberculoid variety of neural leprosy only by microscopical examination which shows round and spindle-shaped histiocytes loaded with the causative bacilli and with fat. The nerve trunks show very similar changes. The lepromun test is negative and the sedimentation rate increased. Lepa fever occurs at times with exacerbation of the symptoms and the appearance of new lesions resembling erythema nodosum the prognosis is bad. On the other hand, in neural leprosy small superficial nerves are involved in relation to skin lesions showing tuberculoid changes but containing extremely few scattered, bacilli local discoloration of the skin and changes in sensation are found. The microscopical characters of these lesions are shown in illustrations. Prognosis in neural cases is comparatively good and spontaneous recovery may ensue they seldom require to be isolated. Isolation however is necessary in all lepromatous cases except very early ones. L. Rogers

FITE G. L. & GEMAR F. Regressive Changes in Leprosy under Promin Therapy. *Southern Med J* 1946 Apr. v 39 No 4 277-82, 1 fig

This important paper records the results of the use of promin in the treatment of leprosy over a period of four years. Daily intravenous doses usually of 5 grammes have been given over periods of three weeks with an interval of one week between the courses. In some cases this treatment was continued for more than 4 years with beneficial results in nearly all. Clinical improvement is slow and reduction in the number of lepra bacilli still slower but progress is nearly always steady and relapses or febrile exacerbations very rare. Repeated microscopical examinations of the skin lesions showed disappearance of inflammatory signs and diminution in the number of bacilli but the latter often did not disappear completely although typical cigar like packets of organisms became extremely rare. The greatest decline in the number of organisms was seen during the fourth year of treatment by the end of which they had disappeared from 21 of 42 patients. With one exception the skin lesions showed extensive evidence of atrophy. The deeper foci of infection showed the greatest diminution in size and in the number of bacilli this may be due to the fact that there is a better blood supply at these sites which brings the drug into closer contact with the bacilli. The lipoids in the affected tissue remain undiminished, and many vacuolated fatty cells persist. Fibrosis is not a feature of regressive lesions.

The drug appears to act by ridding the blood vessels of lepra bacilli and so preventing their spread throughout the body to form new and progressive

lesions. There is little evidence that promin destroys the bacilli in the tissues but they gradually decrease in the old lesions in accordance with the self-healing tendency of leprosy. This explains the slowly beneficial action of the drug. The absence of acute reactions strongly suggests the destruction of the organisms in the blood and the prevention of their dissemination through the body as the essential action of this treatment and their gradual reduction in the tissues to the point of final disappearance as was observed in 10 out of 32 cases treated for four years. A still more powerful bactericidal agent is required for the chemical destruction of bacilli within the tissue cells and especially in the globi laden with the organisms. Chemotherapeutic research with drugs of allied composition seems most likely to furnish this requisite.

L. Rogers

DE WILDEMAN E. A propos de médicaments antilépreux d'origine végétale. V Des "Ephedra" et de leur constitution chimique [Drugs of Vegetal Origin used in Leprosy. The Chemical Composition of Derivatives of Ephedra.] *Inst Roy Colonial Belge—Bull. des Sciences* 1945 v 18 No 2 393-412. [Refs. in footnotes]

The author first discusses the history of the study of plants of the genus *Ephedra* in different parts of the world—these plants yield ephedrine and closely allied alkaloids which are used chiefly in the treatment of asthma, but have occasionally been tried in leprosy. Thirty-one botanical varieties are enumerated in alphabetical order with brief notes of work on those which have been investigated, and suggestions that have been made for their medicinal use. Drugs of this series have been used in China for many centuries, but varieties are met with in India, North Africa and America. Mention is made that preparations from these plants have been used in leprosy but no evidence is given relating to results obtained regarding which the author states that it is difficult to form any conclusions. This paper has therefore little medical interest.

L. Rogers

### HELMINTHIASIS

ALVES W. The "Public Health Cure" of Bilharziasis with One-Day Course of Antimony. *South African Med. J.* 1946 Mar 23 v 20 No. 6, 148-7

A modified form of the intensive treatment of bilharziasis devised by the author [this *Bulletin* 1945 v 42, 815] and by ALVES and BLAIR [this *Bulletin* 1946 v 43 344] is described in this paper.

A group of 131 Africans bilharzia-positive by a cercarial antigen skin test was divided into three groups, each of which was treated under a different dosage scheme with sodium antimonyl tartrate by the slow-injection method previously described as follows—

- |         |  |
|---------|--|
| Group A | 6 grams sodium antimonyl tartrate (S.A.T.) in three doses of 2 grams at four-hourly intervals. |
| Group B | 7½ grams S.A.T. in three doses of 2½ grams at four-hourly intervals.                           |
| Group C | 8 grams S.A.T. in four doses of 2 grams at three-hourly intervals.                             |

The treatment thus occupied only one day. No marked reactions occurred, nor was there any obvious difference between the groups receiving different doses.

The S.A.T. solution was prepared as follows —

Tap water	2,000 cc
Glucose B.P	100 grammes
Sodium chloride A.R	17 grammes
S.A.T. powder B.P	q s. to make either 2 grains or 2½ grains per 10 cc solution

Dissolve filter through paper and autoclave at 120°C. for 20 minutes in 3 000 cc. flasks. Distribute under sterile conditions into sterile vacoliter bottles fitted with two-hole rubber stoppers. Seal stoppers with 6-in squares of previously boiled thin oilskin—similar to jaconet—and tie down. Store in cold room at 4°C

The used vacoliter bottles would not stand autoclaving when filled, but were sterilised without damage in the hot-air oven at 160°C. for one hour. Hence the necessity for autoclaving the solution in flasks and transferring it. The rubber stoppers were boiled with the oilskin squares.

For use the oilskin covering a hole in the rubber stopper was wiped with alcohol and pierced with a syringe needle and the tip of the syringe (minus needle) was inserted when 10 cc could readily be withdrawn. The hole was then covered with sterile cotton wool soaked in alcohol.

Ten cc. of the solution contained either 2 grains or 2½ grains of S.A.T. and no further manipulation was necessary.

These solutions were used up to seven weeks after their preparation and storage and there was no evidence of deterioration to toxic material.

The drug cost of treatment was ½d. per patient.

Urines and stools of every patient were examined two weeks and four weeks after treatment. Seven were passing a few dead eggs on the first examination and one on the second examination but in none were living eggs found.

The significance of this treatment lies in the fact that it provides a rapid method of disinfecting an infected population for a time at least which if used in conjunction with snail destruction should prove to be a valuable weapon in anti-bilharzial campaigns.

J J C Buckley

CAIRO MINISTRY OF PUBLIC HEALTH MEDICAL AFFAIRS Annual Report of the Bilharzia Snail Destruction Section 1943 (BARLOW C. H. (Expert) & ABDEL AZIM, M. (Director) 27 pp 3 maps (2 folding) 2 diagrams & 1 graph. 1946 Cairo Govt. Press

This report consists mainly of an account of the activities of the Snail Destruction Section during 1943 and the first part of 1944.

The methods of snail eradication which are summarized briefly remain essentially the same as those described in the 1942 report [this *Bulletin* 1945 v 42, 1017] and consist of a preliminary survey of canals and drains to note the location and numbers of snails which is followed by treatment of the infested parts by means of (a) clearance of weeds and snails by mechanical methods such as nets, diggers, manual labour and (b) sulphation by means of copper sulphate.

The progress of the campaign in Fayoum Province is reported upon and its success is indicated by a comparison of the 1942 ratio of the number of infested streams to the number surveyed, with the same ratio in 1943. This shows a reduction from 25 per cent to 12 per cent.

The Fayoum campaign was succeeded late in 1942 by a similar one in Giza Province. The topography of this area is described, and for the purposes of

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survey and treatment the province was divided into 14 areas 11 on the west and 3 on the east of the Nile. In 1943 4 111 streams were surveyed and 1 818 (39 per cent) were found to be infested with snails. In 1944 after treatment the percentage of infested streams fell to 22 per cent. The results of the work are also expressed by an estimation of the snail populations in infested streams before and after treatment. Thus, before treatment 13,688 *Bulinus truncatus* were collected by dipping in infested streams [presumably with the standardized collecting nets described in the previous report]. This number represents an average of 63 snails in 100 dpps. After treatment the average fell to 37 snails per 100 dpps. Only two of the 14 areas were infested with *Planorbis boissyi*. The average number of this species per 100 dpps was 125 before treatment and five after treatment.

Concerning the Dakhla Oasis the field of a series of anti-bilharzial measures between 1928 and 1935 some comments are made upon the results of a mission which revisited this area in 1943.

A summary of the results of research work having a bearing on snail destruction is included in the report and is described under the four headings: (1) Seasonal variations in the snail population of the fresh-water streams of Egypt. (2) Observations on the distribution of *Bulinus* and *Planorbis* snails during the winter closure 1943-1944. (3) Palm leaf traps in main canals and drainage. (4) Random examination of *Bulinus* and *Planorbis* snails for schistosome infection in Giza Province.

A comprehensive map illustrates the scope of a projected 6-year plan for snail eradication along the course of the Nile, from Aswan down to and including the delta.

J J C Buckley

VERSIANI V. MARTINS, A. V. & SOBRINHO O. P. Esquistosomose mansônica no estado de Minas Gerais. I—Município de Belo Horizonte. [Infestation with *Schistosoma mansoni* in the State of Minas Gerais.] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais* 1945 v 1 71-80 3 figs. [28 refs.] English summary

The existence of *S. mansoni* infestation in Minas Gerais has been known for more than a quarter of a century. The authors have lately examined the faeces of about 1 per cent of the population of 38 municipalities in the State, choosing in particular children of school age 7-15 years. The method utilized was to take about 2 gm of the faeces in a Borel flask emulsify with a little water and rapidly filter through a metal sieve of 80-100 meshes per sq. cm. into a conical glass. This was allowed to settle for 20 minutes. Fifty cmm. were then withdrawn with a pipette from the bottom of the sediment and examined under low power. Except for better identification of doubtful elements only one examination was made of each sample.

An average of 88 samples was obtained from each of 24 schools, 2,352 altogether. 294 or 12.5 per cent were positive. Of 733 girls 47 (6.4 per cent) of the 1 819 boys 247 (15.23) were positive. 1 234 were from whites and 142 (11.5) were positive among these. 1234 were from blacks, 40 (12.08) and of 787 mulattoes 112 (14.23) were positive. Those of the poorest class were most infected and the rate rose steadily with age from 7-14 per cent. at 8 years to 25 per cent. at 15 years, the intermediate rates being 11.02 13.13 18.19 17.42 and 23.45 per cent. Again, the highest infestation rate was in those living in rural zones. Thus, of 381 town-dwellers 33 were positive (8.6 per cent.) of 1 888 living in the suburbs 225 (12.04) of 103 rural 38 (34.9) were positive.

H. Harold Scott

OLIVEROS NAVA B Estudio estadístico del Servicio Antibilharziano de El Valle Centro de Educación Sanitaria [Statistical Study of the Anti-Schistosomiasis Service in the El Valle District (Venezuela)] *Rev Sanidad y Asistencia Social* Caracas, 1945 Oct-Dec. v 10 Nos 5/6 667-86 5 graphs

The author has analysed the histories of 1,358 patients suffering from infestation by *Schistosoma mansoni*. The commonest reasons for the patient applying for treatment were headache dysenteric symptoms and abdominal pain with general malaise the chief symptoms were malaise and headache in 54-58 per cent and general debility in 53 per cent. Blood and mucus in the stools were seen in only 14 per cent. Enlargement of the liver was present in 58 per cent of the spleen in 63 per cent but the latter was palpable in 15 per cent only the enlargement in the others being by percussion only [enlarged upwards]. More than half the cases (830 or 63 per cent.) occurred in El Valle and 184 (14 per cent.) in El Tuy. Fifty other localities are mentioned but generally few in each only three had more than 50 and 12 had only two cases.

Treatment has been by tartar emetic, starting with 0.03 gm. The total dosage ranged between 1.2 and 1.8 gm. in 656 cases 489 required a second course and 73 a third. Other drugs were tried such as Neostan [? Neostam] Repodral and Stibamine [? Stibamine glucoside] but the numbers of patients to whom these were given are not stated nor is there any mention of dosage. All that is said of them is that Repodral has the advantage of being given intramuscularly and Stibamine orally. Neostan is not referred to again.

H Harold Scott

MAGATH T B & MATHIESON D R. Important Factors in the Epidemiology of Schistosomiasis in Leyte. *Amer J Hyg* 1946, Mar v 43 No 2 152-63 5 figs.

The authors attempted to evaluate the factors responsible for the spotty distribution of schistosomiasis in Leyte. They give an account of the ecology of the snail intermediary *Schistosomophora* (*Oncomelania*) *quadrasii* whose habitats are confined to certain types of water but have a wider distribution during some months in the year. Typically they inhabit the margins of slowly moving water in small creeks where shade is abundant. They were not found in marshy land periodically flooded with sea water in large rivers where the flow is rapid and the banks are sharply defined by steep sides without adjacent swamps in ditches with impermanent water or water exposed to the sun in stagnant water nor in large slow flowing rivers.

The factors governing the localization of the disease were critically examined in Palo a village of high endemicity. [The value of the detailed description of the topography of this place would be greatly enhanced by a sketch map.] The conclusions reached are that snails become infected mainly in the immediate neighbourhood of defaecation sites that human infections may occur at any season but that there may be a strong seasonal incidence that the disease in Leyte is not occupational but is essentially one of childhood that of the reservoir hosts pigs are more important in infecting snails than are dogs and that wild rats are of little importance in this respect.

The determination of the exact type of water in which people may become infected is of great importance. Considerable space is devoted to a discussion of this problem and to the possibility of contracting the infection in large bodies of water the trend of the authors argument is against this possibility. [See also this *Bulletin* 1945 v 42 1018 1946 v 43 350.]

J J C Buckley



MAGATH T. B. & MATHIESON D. R. Factors affecting the hatching of Ova of *Schistosoma japonicum*. *J Parasitology* 1946 Feb. v 32, No 1 64-8.

The functions of development and hatching in the case of *S. japonicum* eggs are very different, and are closely inter related with the different physical environments which characterize the mammalian body and the exterior. While the eggs can develop at body temperature and in the normal salinity of the body either of these conditions will prevent them from hatching. On leaving the body they are released from the influence of these inhibiting factors and hatch readily at the lower temperature and salinity usually encountered in tropical waters if a third factor a sufficiency of oxygen is also present. The experiments described in this paper were designed to determine the factors which prevent *S. japonicum* eggs from hatching within the tissues or in the faeces of the definitive host.

It was found necessary to dilute the faeces with water until much of the putrescent material had been disposed of to obtain a large hatch of miracidia. Hatching continued for several hours and then fell away when the water became foul. Active hatching was renewed when the water was aerated with a bicycle pump or a stream of oxygen. Observations on temperature effects showed that eggs remained viable but would not hatch up to 9 days at 18°C. The optimum hatching range was 25°C to 31°C. and at higher temperatures it was inhibited. No hatching took place in the presence of sodium chloride concentrations as small as 0.7 per cent.

The miracidia were subjected to a gradually increasing temperature (0.5°C. per minute until 37°C. was reached) and it was noted that their most rapid motion was at 33°C. Thirty minutes exposure to 37°C. was usually fatal. Two minutes exposure to a 1.3 per cent. solution of sodium chloride was fatal, but the eggs survived for 1 hour in a 0.66 per cent. concentration and after an hour in a 0.2 per cent. concentration they were apparently normal and might infect the snail intermediate.

J. J. C. Buckley

FAUST E. C. WRIGHT W. H. McMILLEN D. B. & HUNTER, G. W. The Diagnosis of Schistosomiasis Japonica. I. The Symptoms, Signs and Physical Findings Characteristic of Schistosomiasis Japonica at Different Stages in the Development of the Disease. *Amer J Trop Med* 1946 Jan. v 26 No 1 87-112 7 figs. (38 refs)

Far Eastern schistosomiasis katayama disease was first recognized in 1847 the clinical picture of the advanced disease was adequately described in 1883 and its causative agent was discovered in 1904. Japanese medical literature after 1883 contains much information on the serology epidemiology pathology and attempted prevention of the condition but there is little or no information on its incubation period and onset. In 1923 there was a report on a group of 40 Chinese boys and an adult American who swam in infected water and were all ill some seriously, one month later. Other outbreaks with less definite dating of the actual infection have been recorded by European and Chinese workers.

Several hundred cases of Eastern schistosomiasis occurred among American troops within a limited period of the invasion of Leyte Island in the Philippines (October 1944). A group of men in a R.A.A.F. construction squadron were also infected there. These two groups of cases were available to the authors for the study of the late incubation the acute and the early chronic stages of the infection. For the purpose of comparison advanced chronic infections were available in natives in hospitals in Leyte and in Mindanao.

The factors governing the severity of the clinical manifestations of infection in the individual include —(a) the intensity of available cercarial infestation

in the infecting water (b) the gross area of skin and particularly of mucous membrane exposed to attack (c) repetition of exposure to infestation and (d) the reaction of the individual patient to the parasites. At the actual time of infection by the cercariae needling sensations may be felt in the skin. A few days later there is an irritating often unproductive bronchial cough which lasts for several days. Two weeks later moderate or severe urticaria may appear overnight and the patient first appreciates that he is ill. Headache mental dullness tiredness and loss of weight and a feeling of fullness and of pain on pressure over the epigastrium then develop chills and sweats occur at night. These symptoms increase until some four to five weeks after the initial infection when there is a sensation of fullness and pain in the right hypochondrium general abdominal discomfort mucous diarrhoea or a bloody dysentery and marked loss of appetite.

The manifestations appear essentially in this order but not all of them are usually encountered in each patient.

The acute stage of the disease sets in when the mature fertilized female worms begin egg laying and the eggs appear in the stools within a few days. The acute stage lasts three or four months and then continues as the early chronic disease. Four types of the acute stage of Eastern schistosomiasis can be distinguished—(1) the fulminating (2) the severe with sudden onset (3) the insidious and (4) the asymptomatic. In type (1) the fulminating death often occurs before a specific diagnosis is reached and in the one case of this type seen by the authors death occurred in spite of immediate antimony treatment begun before a parasitological diagnosis was made an autopsy showed a massive parasitic infection which had caused an overwhelming intoxication with the metabolites of the worms and their eggs.

In type (2) the severe with sudden onset the appearances 4 to 5 weeks after infection are those of an undiagnosed fever urticaria angioneurotic oedema gastrointestinal distress acute diarrhoea dysentery dengue infectious hepatitis or an upper respiratory infection. Within 81 days of first infection 61 per cent of those found to be infected in one unit had been admitted to hospital severely ill 71 per cent of these infected men had eosinophilia of less than 10 per cent and one patient had 90 per cent eosinophilia. More detailed clinical accounts of these cases are to be published. Two new features relatively common in these severe military cases were nuchal rigidity (soreness and stiffness of the neck) and the development of yellowish nodules on the mucosal surface of the lower sigmoid colon and adjacent part of the rectum. The yellowish nodules were slightly elevated papillae 1-3 mm in diameter which on scraping were found to contain eggs of *S. japonicum*.

In type (3) the insidious infections a gradual development of symptoms and signs took place over a period of one to three months after the usual incubation period. Several such cases were seen in the military groups and difficulty was experienced in diagnosis owing to the mildness of the manifestations. This was even more the case in type (4) asymptomatic infections where the diagnosis was made by routine stool examinations.

The complications of Eastern schistosomiasis encountered were (a) extension of the lesions from the abdominal viscera to other organs and tissues of the body and (b) secondary infections or disease processes. Extension of the lesions by the carriage of eggs to the lungs was seen in one case in other cases eggs were transferred by an unexplained mechanism from the portal circulation to the systemic circulation and lodged in end-arterioles of the toes the skin or the central nervous system. The complicating infections encountered included malaria tuberculosis amoebiasis and other diseases of common occurrence in the tropics all of which may obscure the clinical picture.

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Passage into the early chronic form of the disease is due to the continued discharge into the body of metabolic products of the parasites and the toxæmia resultant on their presence. The accumulation of the very large numbers of eggs produced by this species which fail to reach the exterior act as foreign bodies particularly in the intestine the liver and the mesentery with the resultant development of the classical changes associated with the advanced stage of the disease may develop in cases of very heavy infestation but more commonly the onset of this stage is deferred for four or five years. In natives subject to repeated reinfection manifestations of the early and the advanced stages are often coincident. In the military cases no significant chronic lesions were observed up to a year after infection these may be expected in untreated or inadequately treated cases in five to ten years time.

The authors record in considerable detail the progress of Eastern schistosomiasis in the eight surviving members of a Filipino family infected in a newly discovered endemic focus of infection in Mindanao and they go on to describe other indigenous cases in the same locality. Features of the Filipino cases were the absence of the nodal rigidity so conspicuous in the American military cases the absence of significant eosinophilia at the times of examination and the absence of the severe and prostrating onset which characterized the majority of the American cases admitted to hospital.

The differential diagnosis of Eastern schistosomiasis is discussed. [This paper contains much information and should be consulted in the original by those interested. See also this Bulletin 1945 v 42, 1018.]

A R D Adams

FAUST E. C. The Diagnosis of *Schistosomiasis Japonica*. II. The Diagnostic Characteristics of the Eggs of the Etiologic Agent *Schistosoma japonicum*. *Amer J Trop Med* 1946 Jan v 26 No 1 113-23 27 figs.

The typical, viable mature ova of *Schistosoma japonicum* are readily identifiable but occasionally plant cells in faeces are mistaken for atypical eggs. A chain of eggs distends the venule in which they have been deposited by the retreating ovipositing female which while egg-laying is grasped and held in position by the male worm. The newly-laid egg is immature but normally matures rapidly and the larva contained in it secretes an enzyme through the shell which aids in the escape of the ovum from the containing vessel and in its migration through the tissues into the lumen of the gut. Back-pressure to the obstructed capillary and the contractions of the bowel wall contribute to this process. Immature or degenerate eggs as well as mature eggs may be passed in faeces and their recognition may present difficulties. Descriptions and of the appearances of the immature and maturing eggs of mature viable eggs and of different types and stages of degenerate and dead eggs of *S. japonicum* voided in the stools of infected dogs and men. Careful search of the stools of infected persons by the skilled laboratory worker will usually be rewarded by the recovery of identifiable eggs particularly if a concentration technique is employed. Even where creamy or yellowish pinpoint nodules at a proctoscope from those cases with creamy or yellowish pinpoint nodules at or below the recto-sigmoid junction will yield a parasitological diagnosis. Where even this fails, if a diffuse intestinal capillary dilatation can be seen the microscopically attempted aspiration will rupture the wall of a capillary and the microscopic specimen of blood which exudes may yield a few eggs.

A R D Adams.

DESPORTES C. La dermatite des nageurs. [Swimmer's Itch.] *Ann Parasit Humaine et Comparée* 1944-1945 v 20 Nos 5/6 263-78 1 fig [24 refs]

During the prolonged dry period of October 1944 the author observed foci of snail-infested water at Indre-et Loire. Twelve per cent of these snails were emitting ocellated furcocercous cercariae. Voluntary exposure of the legs on two occasions in infested water resulted in a dermatitis which is described in detail. The beneficial effect of cryotherapy [the use of cold] in alleviating the pruritus is recorded.

In the subsequent section of this paper the literature of swimmer's itch is reviewed and a general study of the disease is set down from the aspects of synonymy definition aetiology pathogeny geographical distribution symptoms clinical picture histopathology diagnosis and individual and general prophylaxis.

J J C Buckley

LARSH J E Jr A Comparison of the Percentage Development of a Mouse Strain of *Hymenolepis* in Alcoholic and Non-Alcoholic Rats and Mice. *J Parasitology* 1946 Feb v 32 No 1 81-3

Seven similar experiments were performed in which a comparison was made of the percentage development of *H. nana* var *fraterna* in alcoholic and non-alcoholic rats and mice. In all but one experiment the alcoholic rats showed percentages of cysticercoid development at least 2-4 times greater than those of non-alcoholic controls. At the same time, alcoholic mice had percentages at least 2-1 times greater than controls in every experiment. These results are interpreted to mean that most young rats as well as mice show a reduced natural resistance to *Hymenolepis* following repeated alcoholization.

LARSH J E Jr The Effect of Alcohol on the Development of Acquired Immunity to *Hymenolepis* in Mice. *J Parasitology* 1946 Feb. v 32 No 1 72-8 [13 refs]

Experiments were carried out to determine the influence of 35 per cent alcohol on reinfection of mice with *H. nana* var *fraterna*. When daily treatment with the drug was not begun until several days after initial infection it had no demonstrable effect on reinfection several weeks later. Thus the action of the immune mechanism stimulated before alcoholization was not interfered with in degree to be measured by the infection method employed. In other experiments in which the drug treatment was given daily for a few weeks before the first infection the results varied with the time interval before reinfection. When this period was one week or 72 hours reinfection was not demonstrated. This probably meant that the alcoholic mice had recovered from debilitation. On the other hand reinfection was demonstrated where only 48 or 24 hours elapsed between infections. In both cases the alcoholic mice showed percentages of cysticercoid development many times greater than those of controls. This indicated therefore that alcohol treatment caused a delayed response to antigenic stimulation but the mechanism for this is as yet unknown.

SANGSTER C. B. Hookworm Disease in Australian Soldiers, with Reports of Cases. *Med J Australia* 1946 Mar. 23 v 1 No 12 385-93 3 figs.

This is an account of hookworm disease among Australian soldiers in New Guinea during nine months in 1943-44 and in Bougainville island during the

first half of 1945 its chief interest is in the detailed description of three acute cases in Bougainville.

In New Guinea the disease was clinically mild and the diagnosis was usually indicated during examination of the blood for malarial or other parasites, or of the faeces for amoebae. In some cases the patient complained of lassitude, abdominal discomfort, dyspnoea on exertion and oedema of the ankles regarded as signs of anaemia. The anaemia was normochromic and normocytic and the haemoglobin was rarely less than 11 gm. per 100 cc. The treatment was oil of chenopodium 1 cc. together with either tetrachlorethylene 4 cc. or carbon tetrachloride 3 cc. this dose was repeated after 8 days if thought necessary. Ferrous sulphate 3 gm. t.i.d. was given for anaemia. A good diet was supplemented in some cases with vitamins B<sub>1</sub> and C.

In Bougainville the disease was also usually mild but there were three acute cases and some others gave the clinical history of the symptoms of the invasive stage. Ground itch usually erythematous and venereal was observed, in different patients from a few minutes to a few days after contact with infected ground. Cough and sore throat with, in some cases bloodstained sputum, appeared after 5 to 7 days and lasted for a month or more. Abdominal discomfort appeared from two to several weeks later. Anorexia, nausea, sometimes vomiting and cramps occurred and there was also intermittent diarrhoea treated as for dysentery with sulphaguanidine without effect however. This history was given by 25 patients.

Diagnosis.—In Bougainville both *Ancylostoma duodenale* and *Necator americanus* were present in New Guinea only *Necator americanus* was found. High eosinophilia was observed in blood examinations an absolute count of over 400 per cmm. being regarded as significant the highest count was 51 000 (85 per cent). Numerous eosinophils (50 per cent) were also seen in the venereal fluid of skin lesions and the sputum also showed numerous eosinophils.

Acute cases.—These three cases are described in detail throughout the illness. There was severe anaemia and persistent diarrhoea with a considerable amount of blood in the stools was present though hookworm ova were not found for several weeks. Repeated doses of the anthelmintic mixture were required and blood transfusions were needed, one patient receiving a total of over 500 ounces in 12 transfusions. This man had a mixed infection of *A. duodenale* and *N. americanus* while the other two had *N. americanus* only. One of the patients developed an abscess of the lung another marrow showed "no lack of 500 hookworms. Examinations of the erythroblastic series showed no lack of maturation and no depression of the erythroblastic series. All three patients recovered after severe illnesses lasting several months.

J. F. CONNOR

DE MEIRA, M. T. V. GONÇALVES, J. & CORREIA, A. de M. F. Sobre um foco de anquilostomose rural autóctona em Portugal. A Rural Focus of Ankylostomiasis in Portugal. 4a Inst. Med. Trop. Lisbon 1945 Dec. v. 2, pp. 67-73. English summary.

KARTMAN, L. A Note on Anopheline Vectors of *Wuchereria bancrofti* in West Africa. (Research Notes. J. Parasitology. 1946 Feb. v. 32, No. 1, 91-2.)

During the early part (January to May) of 1944 the author dissected *Anopheles gambiae* and *A. funestus* caught in four native villages situated within 12 miles eastward of Dakar, Senegal, French West Africa. The results are seen in the table.

TABLE I  
W bancrofti in anopheline mosquitoes from four native villages

Date (1944)	Village	Host	Number Dissected	No filaria found in					Number Infected	Per cent Infection
				Cut	Abdomen	Thorax	Head	Proboscis		
1-15 to 5-17	A	<i>A. gambiae</i>	79	15	0	58	0	1	39	49.3
1-21 to 5-17	B	<i>A. funestus</i>	351	24	0	63	0	0	65	18.5
1-17 to 5-15	C	<i>A. gambiae</i>	23	3	0	2	0	0	3	13.0
1-17 to 5-15	C	<i>A. funestus</i>	82	0	0	2	0	1	2	2.4
5-30 to 6-10	D	<i>A. gambiae</i>	72	61	0	44	9	0	39	54.1
	D	<i>A. funestus</i>	223	28	0	18	0	0	41	18.3
	D	<i>A. gambiae</i>	290	19	3	44	4	0	56	28.0
	D	<i>A. funestus</i>	90	2	3	7	1	0	9	10.0
	D	<i>A. gambiae</i>	374	88	3	148	13	1	137	36.6
Total		<i>A. funestus</i>	740	52	3	90	1	1	117	15.0

These two species were predominant throughout the year far outnumbering all other mosquitoes including *Culex fatigans*. The author states that it has been suggested that *A. funestus* has a lower infection rate than *A. gambiae* because being a smaller mosquito it takes less blood at a feed than *A. gambiae* does. J F Corson

BEHN A W & HAYMAZ J M Jr The Course of Filariasis after Removal from an Endemic Area. Amer J Med Sci 1948 Apr v 211 No 4 385-94 3 figs (13 refs)

A report on the condition of men from the American forces invalided with alleged filariasis from Tonga tabu, an endemic area of Bancroftian filariasis on their arrival in the United States in the latter part of 1943 has already appeared in this Bulletin 1945 v 42, 1020. The present paper is an interim report on the progress of these men (Group A) two years later. It also contains information on a second group (Group B) of 145 men who were exposed to possible infection in Woodlark Island (off New Guinea) and on a further group (Group C) of 32 men who had never been in a filaria endemic zone. Woodlark Island has been shown to harbour the infection. In the Tonga tabu cases (Group A) parasites were demonstrated in very few men other laboratory tests were unhelpful and the diagnosis of filariasis was essentially clinical. In the 532 men comprising this group the authors consider that only 186 really had filariasis and that 336 were free from the infection. The intradermal test with a *Dirofilaria immitis* antigen proved of doubtful value in differentiating the uninfected from the infected as false positive reactions were obtained even in the controls (Group C). A history of one or more attacks of mononucleosis (fever lymphadenopathy and retrograde lymphadenitis) with swelling lasting at least one day was regarded as convincing evidence of an infection. Adenopathy alone was of little significance as it was extremely common in the forces in the Pacific islands. In infected persons the symptoms and signs decrease with the passage of time and most of the infected Group A cases were free of symptoms 20 months after leaving the endemic area.

The authors analyze in some detail the clinical findings among the infected and the uninfected men in Group A and compare them with those encountered in the 145 Group B men from Woodlark Island whose infection at best was problematical. They find a striking similarity in the clinical manifestations such as swelling of limbs or the scrotum and adenopathy in the three groups. Owing to the fact that most physicians lacked acquaintance with the disease a diagnosis of early filariasis was often made on quite inadequate grounds even in men who could never have been exposed to infection. The psychological complications of the diagnosis are considerable in view of the ill-founded fears it engenders and the lack of any specific treatment. The longer an ill-founded diagnosis is allowed to continue the greater the difficulty in restoring the patient to full normality. A R D Adams.

WOLFE H. R. I & SCHOFIELD A L A Case of Filarial Funiculitis. Brit. J Surgery 1948 Apr v 33 No 132, 395-8 3 figs.

An American Naval Air Gunner aged 25 was stationed in tropical Africa from March, 1942 to May 1944 he arrived back in America on February 10th 1945 and was at once sent to hospital as a case of suspected strangulated

inguinal hernia. On the preceding day he felt a stab of pain in the left groin which he thought was caused by the pressure of his parachute harness as he climbed down from an aeroplane to the flight deck of his ship.

On admission his temperature and pulse rate were normal. The left side of the scrotum was indurated and oedematous but the testicle and epididymis felt normal. The cord was thickened and tender up to the external abdominal ring. He had no other symptoms and torsion of a testicular hydatid or acute funiculitis of unknown aetiology was diagnosed and operation advised.

The cord and testicle were explored through a left inguinal incision. Between the external abdominal ring and the testis the cord had expanded into a firm fusiform mass about the size of a walnut. On incising the tunica vaginalis the testis and epididymis appeared normal. The coverings of the cord were incised and examined. The vas deferens was inflamed and nodular and on its surface were some discrete yellowish nodules 0.5-3 mm. in diameter which on microscopic examination were seen to consist of lymphoid follicles packed with eosinophils and they showed marked lymphangiectasis. The pampiniform plexus was engorged and some of its branches in contact with the inflamed vas were thrombosed. An enormously dilated and varicose lymphatic was found running down to the upper pole of the testis. Through its thin wall the wriggling, white hair-like coils of a worm were seen. It was excised and the worms were identified as *Wuchereria bancrofti*. Convalescence was uneventful and the patient left hospital three weeks after the operation.

J F Corson

CULBERTSON J T ROSE H M & OLIVER-GONZALEZ J Chemotherapy of Filariasis due to *Wuchereria bancrofti* with Neostibosan. *Amer J Hyg* 1946 Mar v 43 No 2 145-51 1 fig

This paper describes the progress of an investigation the earlier stages of which have already been reported [this *Bulletin* 1946 v 43 54 & 354]. Briefly 35 patients with microfilariae in the blood were given neostibosan. Twenty (Group I) were given 4.6 to 10.5 gm in 33-54 days. Ten (Group II) were given the same course as Group I but as this seemed relatively ineffective they were treated again 9 months later with 5.9 to 12.5 gm during 14 days. Five patients (Group III) were treated intensively receiving 9.5-15.5 gm. in 13-14 days. The initial dose was 0.1 gm. injected intravenously later this was worked up to two or three injections each of 0.5 gm. per day.

Of the patients in Group I 15 lost all their microfilariae in various periods up to 15 months after treatment. In three patients the microfilariae were greatly reduced in 15 months and in two patients there was little change in 9 months. In the 10 patients of Group II who had resisted the first course three lost their microfilariae in five months, in six the microfilariae were much reduced, and one showed only slight change. In Group III two patients became microfilaria negative in six months and three lost at least half their microfilariae.

Among 15 control patients none became microfilaria-negative in 14-17 months and 11 showed considerable increase in the number of microfilariae present in the blood. Toxic reactions in the treated patients were relatively light although half the patients experienced nausea and vomiting, two had severe nausea, anorexia and other symptoms but it was not necessary to stop the drug in any patient. None of the treated patients has shown any sign of the development of elephantiasis although such a hazard, as a result of treatment has been suggested by some investigators. It is believed that neostibosan kills the adult worms leaving the microfilariae to disappear slowly from the circulating blood because their number is no longer replenished.

F Hawking



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PUNG SOLAWES M. FORTES A. & ANTONIO QUINTAN. [La onchocercosis en el estado de Chiapas. [Onchocerciasis in the State of Chiapas, Mexico.] Reprinted from *Rev. Salubridad y Asistencia* 1945 July & Aug. No 10 30 pp. 19 figs.

Investigation into the ocular complications of onchocerciasis was carried out in 1945 under the auspices of the Pan-American Sanitary Department, in a part of the State of Chiapas, Mexico.

This investigation into the ocular complications of onchocerciasis was carried out during February 1945 under the auspices of the Pan-American Sanitary Bureau and the Mexican Health Department, in a part of the State of Chiapas.

This investigation into the ocular complications of onchocerciasis was conducted during February 1945 under the auspices of the Federal Bureau and the Mexican Health Department, in a part of the State of Yucatán where onchocerciasis was known to be endemic.

Ninety three cases (elsewhere the number with nodules is given as 89) or by biopsy tests. One had superficial punctate keratitis regarded as characteristic of the infestation although no nodules were present. Of the 93 there were 64 males 29 females 78 were of mixed race 13 were natives 4 were not noted [but no mention is made of the relative constituents of these in the population of age and 18 below 10 years 17 in the third decade [by ages the total of cases amounts to 92 other discrepancies occur in the tables for example in one of the cases over 10 years total 73 not 76] Onchocerca dermatitis present or absent was noted in 19 cases biopsy was positive in 70 (76 per cent) negative in 18 (20.4 per cent) of 88 so tested.

The longest section of this contribution is devoted to the ocular symptoms of the disease in the eye but without clinical signs. In most of the cases 2-9 years after the earliest indications of the disease 57 gave a positive biopsy finding. Sixteen presented the disease in the eye but without clinical signs.

at no mention is made of the racial incidence in the past was noted in 19 cases of 83 so tested. The longest section of this contribution is devoted to the ocular symptoms present in this disease. Seventy of the 83 had demonstrable clinical signs, one had the embryos in the eye but without clinical signs. In most of the patients eye symptoms appeared in 7-9 years after the earliest indications of infestation and of the 70 45 had nodules and 57 gave positive biopsy findings. Microfilariae were found in the eyes of 29 patients. Sixteen presented the typical symptoms of burning, smarting and the sensation of the presence of a foreign body. Affection of the cornea was seen in 60 of the 101 in 27 glaucoma secondary to onchocerciasis occurred in one. The commonest lesion of the cornea was a punctate superficial keratitis and refractive findings were the sites usually bilateral and symmetrical. Some of the corneal deposits were the sites of dead microfilariae and it may be that the death of the embryos was the real cause of the keratitis. This keratitis, strange to say affected but slightly the acuity of vision. Of 81 examined, the vision was 10/10 in 45 8/10 in 9. The vitreous evolves very slowly but seriously affects visual acuity. Of 18 with this complication only two had normal vision, one had not even perception of light and 14 others had vision 1/20 or less. Lesions of the fundus were of light and the greater frequency in African patients is ascribed to the co-existence of other diseases such as tuberculosis, syphilis or trypanosomiasis. An additional reason must not be left out of account. Patients in African records had had no treatment whereas the majority of those studied in the present investigation had undergone periodical removal of nodules.

H Harold Scott

Cause of Malaria Parasitosis. J Bone

153-6 3 figs

sensation pain

H Harold Scott

CORRECTION: Trichinosis as a Cause of Myalgia Parasitologica. J Bone & Joint Surg 1948 Jan v 28 No 1 153-6 3 figs

Trichinosis as a Cause of Meralgia Paresthetica  
Joint Surgery 1948 Jan v 28 No 1 153-6 3 figs

Meralgia paresthetica is characterized by alteration of sensation, pain or diminished sensation on the antero-lateral aspect of the thigh on walking or by contact with clothing and is ascribed to neuritis or to pressure on the external femoral cutaneous nerve. It has been found associated with pressure from a belt or corset. The nerve runs close to the anterior superior iliac spine and passes over or under the sartorius and pressure may thus be caused by an abnormally placed fibrous band.

The case here described is that of a man 42 years of age who had suffered for 4 years from numbness of this area with pins and needles and hot and cold sensations. Walking increased the symptoms and often caused pain. Operation revealed that the nerve in question was being compressed by a dense fibrous band. Immediate relief was obtained by excision of this band. Section of the tissue removed revealed numerous cysts of *Trichinella spiralis* but none of them calcified. A history was obtained of the patient having a year before the onset of these symptoms eaten pork and suffered after the meal from fever and diarrhoea. [There is no doubt of the association of the trichiniasis with the symptoms but to what degree the parasite was aetiologicaly responsible is less certain. The fibrous band was present but this may be so in the absence of any *Trichinella spiralis*.] H. Harold Scott

AYERA J W YOW E M HARRELL G T & FOWLER Elizabeth B. An Attempt by Feeding to Induce in Animals Reactivity to *Trichinella spiralis* in the Absence of Infection. Amer J Trop Med 1946 Jan v 28 No 1 125-31

HARRELL and HORNE. *Bulletin of Hygiene* 1945 v 20 469 found a significantly higher incidence of positive skin tests done with *Trichinella* antigen among patients in tuberculosis sanatoria and in hospitals for mental disease than among subjects in general hospitals. The length of stay in the institution seemed to be significant but that study provided no evidence of the existence of unrecognized institutional epidemics of trichiniasis. THIBERGE (*J Allergy* 1944 v 15 298) reported that antigens contained in pollens can cross the mucosal barriers of the intestine and can cause symptoms in allergic subjects. If the sensitizing agent can cross the intact mucosa ingestion of meat containing killed larvae of *Trichinella* might cause sensitivity. Cooking might denature the protein of *Trichinella* but meat frozen to make it non-infective could be so incompletely cooked that the antigen might be unaltered. This might explain the high incidence of positive skin tests done on subjects in institutions. The present study was made to find out whether positive skin tests could be produced in animals not infested with *Trichinella* by the ingestion of killed *Trichinella*. It showed that this did not happen and that the hypothesis just suggested did not explain the high incidence of positive skin tests in subjects in institutions. For details of the experiments the original should be consulted.

Discussing their results the authors say that SPINDLER and CROSS (*Proc Helminth Soc Wash* 1939 v 6 37) reported that skin sensitivity could be acquired by hogs by eating scraps of pork containing non viable larvae of *Trichinella* and that SCHWARTZ in a personal communication told them that hogs fed with cooked trichinized meat for several weeks gave weakly positive intracutaneous reactions to *Trichinella* antigen although no trichinellae could be found in them. The present authors have been unable to reproduce this phenomenon in the guinea pigs and rabbits which they used. The skin tests and flocculation tests recorded in this paper failed to show that animals fed with trichinized meat reacted to the antigens nor did meat containing *Trichinella* larvae killed by freezing in order to avoid denaturation of the *Trichinella* protein produce positive skin or flocculation reactions. The present authors have not tried to find out whether the digestive juices of herbivorous animals can inactivate antigens of killed *Trichinella* although THIBERGE (*loc. cit*) states that ingested pollen is inactivated by the gastric digestion of man. The authors think that because the degree of allergy in trichinosis individuals is high the passage of undenatured *Trichinella* antigen across the mucosa

might cause vague symptoms which might be attributed to allergy to pork but are really due to allergy to the parasite contained in the meat. This mechanism might be responsible for the high incidence of *Brucella* skin tests because antigen which has passed the mucosal barrier might produce sensitivity without infection.

Contrary to reports in the literature [see BACHMAN this *Bulletin* 1929 v 28 551] the authors were unable to produce strongly positive skin reactions to 1:200 dilutions of *Trichinella* antigen in guinea-pigs known to be infected. They consider that rabbits are better than guinea-pigs for skin and flocculation tests. The most clear-cut skin reactions were however obtained in the infected dog used and the authors suggest that rabbits, or preferably dogs, should be used rather than guinea-pigs for future skin tests. The authors cannot explain why the flocculation tests were not clearly positive in the infected guinea-pigs. No precipitin tests were done for comparison with them but the flocculation test gave positive results in infected rabbits and detected an extremely mild degree of infection in one rabbit. The technique of this test is however tricky and needs large amounts of dried and powdered larvae. In its present stage of development it is probably not applicable to large-scale work, although it gives promise of being useful for the diagnosis of suspected cases.

G. Lapege

DRACHMANS, R. & COTTET, J. Etude expérimentale des acides et des sels biliaires dans l'oxycure [Experimental Study of Bile Acids and Bile Salts in Enteroblastia.] *Bull Soc Path Exot.* 1945 v 38 Nov 11/12, 341-4.

## DEFICIENCY DISEASES

HUGHES W. Kwashiorkor and Ariboflavinosis. *Trans Roy Soc Trop Med & Hyg* 1946 Apr v 39 No. 5 437-48 8 figs. on 4 pls. [18 refs.]

In Lagos three fairly well-defined syndromes of malnutrition may be distinguished—simple ariboflavinosis, kwashiorkor and nutritional achromotrichia. These are not rigidly distinct—simple ariboflavinosis, characterized by lesions of mouth, tongue and external genitals, is commonest among adults. Rare cases, however, occur in children and these constitute a link between the adult syndrome and kwashiorkor. Achromotrichia appears to be a separate condition in which muco-cutaneous lesions are minimal. It may be present in some cases of kwashiorkor but alopecia is more common. It is suggested that nutritional achromotrichia may be caused by pantothenate deficiency.

The description that follows is based on the findings in 65 cases of kwashiorkor. Nearly half of these patients were two years old or less, although some cases were seen up to the age of 9 years. With increasing age the mortality and severity declined and the condition merged into the simple ariboflavinosis of adults. It is argued that in kwashiorkor the epithelial lesions are essentially similar to those of adult ariboflavinosis, but more widespread, and more severe. The two conditions may perhaps be best contrasted in a table constructed from the author's data.—

	<i>Adult Ariboflavinosis</i>	<i>Kwashiorkor</i>
Mouth	Glossitis cheilosis angular stomatitis	Glossitis cheilosis angular stomatitis
Face	Seborrhoeic lesions in naso-labial folds at canthi etc.	Fissures in naso-labial folds at canthi, above ears
Perineum	Dermatitis of scrotum	Scaling and exfoliation of prepuce scrotum, vulva and whole of perineum. Fissures and depigmentation.
Other parts	Typically no change	Desquamation and exfoliation on extensor surfaces of limbs dorsa of hands and feet, tips of nose and ears. Depigmentation and fissuring in flexures.

Many of the lesions listed above are illustrated by excellent photographs. Microscopically the skin showed parakeratosis and acanthosis.

Other features of the disease were lethargy, anorexia, muscular wasting, bradycardia, anaemia, oedema, and signs of dehydration with oliguria. In four cases there was an abrupt and unexpected lapse into coma and death. At post mortem examination the outstanding feature was fatty infiltration of the liver. The more the cases approached the typical the more intense the fatty change.

The author points out that in experiments on riboflavin-deficient dogs SEBRELL [*Bulletin of Hygiene* 1930 \ 5 374] observed sudden death in coma, and a fatty liver post mortem. These findings supported the view that kwashiorkor might be a result of ariboflavinosis. However the results of treatment were disappointing. riboflavin in doses of 10 mg parenterally rapidly cured the lesions of mouth and perineum, but it did not prevent death. Crude liver extracts seemed to produce some beneficial effect particularly an improvement in appetite. In many cases death was precipitated by concomitant disease such as malaria, tuberculosis or septicaemia.

Summarizing the author states that it is something if we can recognize and follow the thread of riboflavin deficiency through the complicated pattern of kwashiorkor. The severe case is probably suffering from many other deficiencies consequent on inanition. Even if the final hepatic lesion is the consequence of inanition and quite beyond the influence of B<sub>2</sub>-complex therapy it will not alter the position from the preventive point of view. It is suggested that for prevention attention should be concentrated on making available supplies of the B<sub>2</sub>-complex and that a practical source of this is food-yeast in a dosage of 10 grammes daily.

[In the treatment of kwashiorkor nicotinic acid has been no more successful than riboflavin. Neither appears to have any effect on the liver lesion. The experimental evidence for the production of fatty liver by deficiency of B<sub>2</sub> vitamins except choline is slender. The liver lesion described by SEBRELL (*loc cit*) appears to be histologically different from that of kwashiorkor. On the other hand there is much experimental evidence that a fatty liver can be produced by protein or amino-acid deficiency and some clinical evidence that a high protein diet has a good effect on the liver in kwashiorkor. The recommendations made here for prevention must be examined in the light of this possibility—that the liver damage is not irreversible, and that it is the result of deficiency of protein or its derivatives. The recommended daily dose of 10 grammes of food yeast would supply 4 grammes of protein.]

J C Waterlow

HUGHES W. Food Yeast in Tropical Malnutrition. *Lancet* 1946 Apr 20 569-72.

Feeding trials with food yeast were carried out on prisoners and lunatics in Nigeria. In both these groups signs of riboflavin deficiency were very common.

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being found in 25-30 per cent. of subjects examined. Four grammes of food yeast were given daily for five weeks to a group of 18 prisoners with severe signs of deficiency. At the end of this time the number with lesions was reduced to five of whom only one was severely affected. During the following three weeks when no yeast was given, six patients relapsed. In a control group of untreated prisoners there was no change in the incidence of severity of the lesions.

In a second experiment, 145 male lunatics received 8 gm. of food yeast daily for seven weeks. The number of cases with signs of riboflavin deficiency fell from 45 to 18 and the severity of the lesions decreased. In a control group of female lunatics who did not get yeast, there was no change in the incidence of lesions, and the severity increased. In a similar trial on prisoners, 9 gm. of yeast were given daily for eight weeks. Out of 64 cases with signs of riboflavin deficiency 58 were cured.

It is concluded that 10 grammes of food yeast daily would be enough to prevent manifestations of riboflavin deficiency in the population of Lagos. This amount of food-yeast contains about 0.5 mgm. of riboflavin.

This estimate is given of the riboflavin content of the average Nigerian diet, so that it is not possible to see how far the recommended supplement of 0.5 mgm. goes towards filling the gap between actual intake and optimum requirement. Adequate nutrition is not necessarily achieved with the correction or prevention of clinical deficiency.]

J C Watkinson

SPRYS T D & MOREY Mabel M. A Clinical Study on the Use of a Protein Supplement in treating Persons with Nutritive Failure. *Southern Med J* 1946 Feb v 39 No 2, 117-21 5 figs.

In the last few years it has gradually though rather tardily been recognized that in the clinical conditions we call deficiency diseases the deficiency is one of several nutrient factors and that these include not only the so-called vitamins—in other words the term deficiency disease is not synonymous with hypovitaminosis. The authors say we are becoming increasingly aware of the extent of the protein deficiency in many diets and its role in nutritive failure. We are studying not only the effect of individual amino acid on persons with deficiency diseases but also the effect of complex concentrated proteins such as hydrolyzed casein.

The case histories of two patients selected from a group of 16 with pellagra and anaemia and oedema are given to illustrate the effect of the latter. The administration of hydrolysates appeared to clear up the oedema and in some cases the cheilosis which had proved resistant to riboflavin.

Apart from the attempt to show experimentally the specific effect of protein hydrolysates on certain symptoms it would appear that these have no advantage over a correct diet containing meat, milk and eggs.

H S Sianis.

GOPALAN C. The "Burning Feet" Syndrome. *Indian Med Gaz.* 1946 Jan. v 81 No 1 23-8

The author gives an excellent description of the syndrome burning feet—Kai erichal, in Tamil—well known to medical men who have had opportunities for making observations among indigenous populations during the past half century. He quite correctly states that the condition should be clearly distinguished from peripheral neuritis and beriberi with which it has often been confused by authors whose observations have not been made with sufficient care.

This article is based on 53 cases 14 males and 39 females from among a poor population living on a parboiled rice gruel and cheap vegetables. Among the women 27 gave a history of parturition within a few weeks of being seen.

In practically all the patients signs of riboflavin deficiency were present—glossitis angular stomatitis angular blepharitis in some superficial keratitis was present in a fair proportion of the males scrotal dermatitis was noted and in the women leucorrhoea was present [no slit lamp examinations apparently were made]

The burning pain commonly began in the region of the ball of the big toe then spread over the sole and sometimes involved the dorsum of the foot and ankle less often the palms of the hands were involved.

Some cases were seen in which excruciating paroxysms of burning pain alternated with freedom from it. Associated with this symptom sensations of pins and needles were complained of as noted by other observers but the two did not necessarily parallel each other.

Hyperidrosis another well known symptom of the syndrome was noted as occurring in the areas of burning pain. On the other hand there was no muscular wasting or tenderness no loss of power no paralysis no spasticity no loss of reflexes no sensory loss of any kind.

There was no response to thiamin or nicotinic acid. Treatment with riboflavin while clearing up the signs of hyporiboflavinosis left unchanged the burning pain syndrome. Rapid improvement and cure however followed upon the daily intramuscular injection of 20 to 40 mgm. calcium pantothenate for 2-3 weeks in 10 cases submitted to the treatment.

In discussing the pathology ('pathogeny') of the condition reference is made to the abridged version of the Lumleian Lectures for 1944 [this *Bulletin* 1944 v 41 862] in the following words. Stannus (1944) has indeed suggested that burning feet is part of the syndrome of ariboflavinosis. [This is of course incorrect as throughout those lectures—entitled Some Problems in Riboflavin and Allied Deficiencies—it was made clear that the syndromes described were due to a hyporiboflavinosis alone or associated with a deficiency of another closely allied factor of the B complex.] In further discussion no fresh data are supplied and no definite conclusions are reached in regard to pathogeny.

H S Stannus

### SPRUE.

SPIES T D MILANES F MENÉNDEZ A. KOCH Mary B & MINNICH Virginia  
Observations on the Treatment of Tropical Sprue with Folic Acid. *J Lab & Clin Med* 1946 Feb v 31 No 2 227-41 4 figs.

Nine patients suffering from tropical sprue were treated, under standardized conditions with folic acid by mouth in dosage ranging from 10 to 200 mgm. daily. The response of those receiving only 10 mgm closely paralleled that of those receiving higher doses and was manifest by a rapid improvement in each patient's feeling of well-being an increase in appetite a gain in weight and strength a decrease in the pigmentation of the skin together with resolution of the glossitis soreness of the mouth and burning of the rectum. This clinical improvement was accompanied by a striking haematological improvement. In all cases a maximal reticulocytosis occurred, the day of the peak ranging from the sixth to the ninth day which was followed by rises in the red cell count varying from 0.50 to 1.21 million per cubic millimeter in 14 days in the patients receiving 200 gm. folic acid, and from 0.46 to 0.71 million in those

receiving 10 mgm doses. The haemoglobin levels of all the patients increased as the erythrocyte counts increased while the leucopenia generally accompanying the macrocytic anaemia decreased. Normal control subjects receiving 200 mgm. folic acid orally for ten days showed no changes in their erythrocyte counts haemoglobin levels, leucocyte counts or in the number of reticulocytes in the four weeks following the administration of the drug. The bone marrow of the patients with sprue treated with folic acid, showed macroscopically a gross change from light red, thick gelatinous marrow to deep red fluid containing discrete clumps of cells and macroscopically the erythroblastic arrest of the disease was replaced by a normoblastic hyperplastic regeneration, with a shift in the ratio of white cells to nucleated red cells from 5:2 to 5:6.

The paresthesiae of the hands and feet were not markedly affected by the administration of folic acid but the oedema disappeared in all but two patients. The diarrhoea followed a variable course, gradually decreasing in most cases, although in some the faeces failed to improve while in others initial improvement would sometimes be followed by reversion for a day or so to copious frothy stools. (See also Series below) F. Mergelroyd.

DARBY W. J. JONES, E. & JOHNSON, H. C. Effect of Synthetic Lactobacillus Casei Factor in Treatment of Sprue. *J Amer Med Ass* 1946 Mar 23 v 130 No. 12, 780-88 7 figs [Refs. in footnotes]

A deficiency syndrome in the monkey characterized by anaemia, leucopenia, diarrhoea, oral lesions, facial oedema, loss of weight and death can be prevented by a factor sometimes referred to as vitamin M, which has been differentiated from nicotinic acid, riboflavin, thiamin, panthothemic acid, choline, para aminobenzoic acid, pyridoxine and inositol. Certain purified liver extracts which were effective in the treatment of pernicious anaemia also failed to prevent the nutritional cytopenia in the monkey. Monkeys deficient in vitamin M respond, however, to the intramuscular administration of small quantities of a highly purified *Lactobacillus casei* factor and the various similarities of vitamin deficiency in the monkey to the sprue syndrome in man led to a test of the efficacy of the newly synthesized *L. casei* factor in the treatment of three patients suffering from sprue.

The patients were maintained on standardized diets devoid of organ meats, and the crystalline *L. casei* factor was given intramuscularly in a dosage of 15 mgm daily. The response of the patients resembled that following the administration of an active liver preparation. Within two or three days all the patients experienced a feeling of improvement. The glossitis was relieved by the fourth or fifth day and simultaneously there was a cessation of the diarrhoea and an increase in appetite. A gain in weight commenced on approximately the fifth to the seventh day, the initial gain apparently reflecting water retention as it was accompanied by demonstrable oedema and haemodilution which disappeared about the twelfth to the fourteenth day. Subsidence of this oedema was followed by a striking increase in weight unaccompanied by water retention. Although the diarrhoea was promptly relieved, stool analyses did not show a return to the normal fat content while furthermore the patients did not exhibit an increase of fat within the gastrointestinal lumen.

The treatment brought about increases in all the formed elements of the blood and the bone marrow which prior to treatment was begun. arrest, returned to normal ten days after administration of this *L. casei* factor will result in a satisfactory response in cases of sprue, pernicious anaemia, macrocytic anaemia of pregnancy and nutritional macrocytic anaemia. Unpublished data.

indicate that the factor is effective only in those macrocytic anaemias with hyperplastic primitive marrow so-called dysplastic and aplastic anaemias failing to respond even though examination of the peripheral blood indicated a macrocytic anaemia.

From the relationship outlined the authors suggest that vitamin M deficiency in the monkey is the experimental analogue of sprue in man. As the term folic acid has been so loosely used they feel that its retention can but lead to confusion and they propose that the group of substances which possess similar haematopoietic activity for primates be referred to as the vitamin M group [see SPIES this *Bulletin* 1946 v. 43 582 SPIES *et al.* above]

The doses given to the patients in these experiments are probably in excess of the minimal amount which would produce a maximal response. A reticulocyte response has been reported in two patients suffering from pernicious anaemia who were given intravenously only 2 mgm. daily and from a comparison of the requirements of chicks for riboflavin and the *L. casei* factor it is suggested that in man the maintenance dose of the *L. casei* factor may be of the order of 0.1 to 0.2 mgm. daily and that the curative dose may be about 1 mgm. daily. No local or systemic toxic effects were however observed from the administration of the material in the doses employed to 12 persons manifesting a variety of blood dyscrasias. [See also this *Bulletin* 1946 v. 43 667] F Murgatroyd

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## HAEMATOLOGY

SPIES T. D. Effect of Folic Acid on Persons with Macrocytic Anemia in Relapse  
*J Amer Med Ass* 1946 Feb 23 v. 130 No. 8 474-7

Folic acid was given parenterally or orally in amounts of 20 mgm. or more daily to 45 patients suffering from anaemia, including 8 patients with nutritional macrocytic anaemia, 8 with pernicious anaemia, 11 with sprue, 3 with anaemia associated with pregnancy, 1 with anaemia associated with carcinoma, 1 with anaemia associated with chronic alcoholic addiction, cirrhosis of the liver and neuritis, 3 with anaemia of undetermined origin, 3 with aplastic anaemia, 3 with anaemia associated with leukaemia, and 4 with iron deficiency anaemia. None of the patients with aplastic anaemia, iron deficiency anaemia, or the anaemia associated with leukaemia showed any improvement but there was a very marked subjective and objective improvement following the administration of folic acid to those suffering from macrocytic anaemias. These latter patients experienced an immediate feeling of improvement together with an increase in strength, vigour and appetite. This subjective improvement coincided with or was followed by an increase in the reticulocytes of the peripheral blood and by subsequent rises in the red blood cell counts and in the haemoglobin content of the blood. This improvement occurred regardless of the mode of administration of the drug. The minimal and optimal doses of folic acid have not yet been determined and there appears to be some variation from patient to patient. It has been found however that while 400 mgm. daily may be administered without untoward symptoms as little as 5 to 10 mgm. parenterally or 10 mgm. orally each day will often produce a maximal haematopoietic response. It has also been found that patients failing to respond fully to 3 to 4 mgm. folic acid daily may respond to liver extract or yeast administered in amounts which supply only 1 mgm. or less of folic acid daily which suggests that the antianaemic factor present in liver extract or yeast may be a combination of chemical substances.

F Murgatroyd



SPIES T. D. VILTER, C. F. CLINE, J. K. & FROMMEYER, W. B. The Substitution of Thymine for Folic Acid in the Treatment of Macrocytic Anemias in Rabbits. *Southern Med J* 1946 Mar v 39 No. 3 269-70 [12 refs.]

It has been shown that thymine (2, 4-dihydroxy-5-methyl-pyrimidine) an integral portion of cells, and occurring as part of nucleic acid, could replace folic acid as a growth factor for lactic acid bacteria provided that other essential substances, including adenine, guanine, or xanthine were present, but the amount of thymine required was 5 000 times as great as that of folic acid. It was suggested that folic acid acts as an enzyme or coenzyme in the synthesis of thymine or a thymine-like compound which is used by the bacteria to form nucleic acid.

If this represents a fundamental biochemical mechanism of cellular activity it is possible that thymine might replace folic acid in the maturation of the cellular elements of the blood, and the amount of thymine required might be of the order of 12.5 to 25 gm. daily, since some patients with macrocytic anaemia respond to as little as 2.5 to 5 mgm. of folic acid daily.

Six patients with nutritional macrocytic anaemia and the anaemia of sprue showed no response to thymine in doses of 5 to 50 mgm. daily for ten days. One patient given 500 mgm. twice daily for six days also showed no response but when the dose was increased to 2 gm. three daily for 14 days a reticulocytosis of 14.2 per cent was reached on the eleventh day and concomitant decrease in the symptoms referable to the glossitis. The erythrocytes also rose from 2.01 million to 2.74 million and the haemoglobin from 6.3 gm. to 9.4 gm on the twentieth day of the treatment with the large dosage. Thereafter without further treatment the reticulocytes subsided but the erythrocytes increased to 2.83 million and the haemoglobin to 10.4 gm while the bone marrow reverted from a condition of megaloblastic arrest to normal.

F. Margatroyd

COOPERMAN, J. M. ELVENJEN, A. McCall, K. B. & REEGANER, W. R. "Folic Acid" Active Compounds in the Nutrition of the Monkey. *Proc Soc Exper Biol & Med* 1946 Jan v 61 No 1 92-7 2 figs. [13 refs.]

A nonite eluate concentrate extractable from yeast or from liver extract, appears to contain at least three factors, namely folic acid necessary for the growth of *Lactobacillus*, also vitamin B<sub>12</sub> necessary for normal feathering in chicks, and vitamin B<sub>12</sub> necessary for normal growth in chicks. A crystalline compound which has properties similar to those of this concentrate, and which has been called vitamin B<sub>12</sub>, can be isolated from liver while a vitamin B conjugate has been isolated from yeast and is active for the chick but has no activity for the bacterium. Upon enzymic digestion, however, this B<sub>12</sub> conjugate becomes active as a source of B for *L. casei*.

A deficiency of folic acid in monkeys leads to a syndrome, a prominent feature of which is leucopenia and experiments showed that crystalline B and a synthetic *L. casei* factor were active in doses of 100γ daily that the B<sub>12</sub> conjugate was less active in doses of 200γ and 300γ daily and that B<sub>12</sub> and B<sub>12</sub> concentrates were inactive as sources of folic acid. The folic acid deficiency also precipitates a deficiency for the monkey anti-anæmic factor which is characterized by lack of growth a suboptimal haemoglobin level and a reversal in the neutrophile-lymphocyte ratio. While B<sub>12</sub> conjugate, B<sub>12</sub>, and the synthetic *L. casei* factor were effective in raising the leucocyte count the addition of whole liver was necessary to correct the neutrophile-lymphocyte ratio the low haemoglobin level, and the loss in weight.

F. Margatroyd

GIBSON, Q. H. & HARRISON, D. C. An Artificial Standard for Use in the Estimation of Haemoglobin. *Biochem J* 1945, 39 No 5 490-97 [15 refs.]

A satisfactory standard for general use in haemoglobinometry should be reproducible, stable, easily prepared and have an absorption spectrum closely similar to that of the blood derivative with which it is to be compared. These requirements appear to be fulfilled by a standard solution of a mixture of organic salts prepared according to the following directions—Weigh out 11.61 gm. of  $\text{CrK}(\text{SO}_4)_2 \cdot 12 \text{H}_2\text{O}$  (Analar) using crystals free from any sign of whitening due to efflorescence, 13.10 gm. of anhydrous  $\text{CoSO}_4$  or the equivalent weight of the hydrated salt and 0.69 gm. of  $\text{K}_2\text{Cr}_2\text{O}_7$  dissolve in about 500 ml of distilled water add 1.8 ml of  $\text{N H}_2\text{SO}_4$  and heat to boiling. Boil for 1 minute cool well and make up to 1000 ml with distilled water. A more precise method of preparing the standard is also described but solutions prepared by the simplified method given above show readings in the absorptiometer in close agreement with those shown by the precise standard. The standard should be stored in a glass-stoppered bottle free from grease and organic material and ethanol or acetone should not be used for drying apparatus used to contain the standard.

For the routine determination of blood haemoglobin pipette 10 ml of a clear solution of 0.1 N NaOH into a dry boiling tube fitted with a loosely fitting ground-glass stopper. Ordinary corks must not be used as they give a colour with the alkali. Pure NaOH (Analar) should be used as some impure samples of NaOH give an opalescence when heated with blood and the solution should be stored in a Pyrex vessel. Add 0.1 ml of blood stopper and mix gently for a few minutes until the solution is clear. Take about the same volume of standard in a similar tube and immerse the two tubes with the stoppers loosened in a vigorously boiling water bath so that the solutions in the tubes are just below the level of the water. Heat for exactly 4 minutes after which at once cool thoroughly by immersion in cold water and mix by inversion. The haemoglobin can then be determined by visual comparison of the two solutions in a colorimeter preferably with a green filter over the eyepiece the haemoglobin value of the standard being taken as 18.0 gm./100 ml. using filters and 16.2 gm./100 ml using unfiltered light. With standardized light and filters the determinations may be made with a photometer or a photoelectric absorptiometer.

The systematic error involved in using the standard as described should not exceed  $\pm 1.5$  per cent i.e.  $\pm 0.2$  gm of haemoglobin/100 ml. in a normal blood and in view of the variability of blood samples from the same individual it would appear that no practical advantage would be gained from a greater degree of precision.

During determinations of haemoglobin by various methods a consistent difference was found between the values calculated from Fe determinations and oxygen capacity measurements of normal blood. The difference was not due to the presence of carboxyhaemoglobin or methaemoglobin nor due to neglect of plasma iron but indicated the presence of some 3 per cent of iron in a non functional form in normal blood.

F. Margatroyd

DEWHURST, A. E. The "Cooke-Ponder" Lobular Neutrophil Count on the East African Askari. *East African Med J* 1946 Feb, 23 No 2 47-50

The usual procedure for classifying the neutrophil leucocytes into their different maturity groups consists of determining the various percentages of

the cells having one two three four and more than four lobulated nuclei as shown in 100 consecutive cells of a thin film stained by Giemsa's method. The criterion of separate lobulation is that either the lobes appear detached or are joined only by a thin filament of chromatin if there is any doubt about the number of nuclear lobes the cell should be classified in the lower class. Various indices are used to express the results of such a count, the commonest being the Arneth Index, which is obtained by adding the percentages of cells in the first second and one-half of the third class. Another method of expression is by the weighted mean of the percentage counts, a figure obtained by multiplying the number of cells in class I by 1 the number in class II by 2, and so on to class V the sum of the figures so obtained being then divided by the total cells counted namely 100. A higher Arneth Index than 58.5 or a lower weighted mean than 2.75 is taken to indicate a shift to the left from the normal for Europeans such shifts have been found in routine surveys of bloods from Egypt Malaya and China.

The present paper records the results of a survey of 500 apparently healthy indigenous East Africans drawn from the following tribes, Jalu Kikuyu Baganda and Mumwami. No significant tribal differences were noticed and for the total survey the results were — neutrophils of class I 14 per cent class II 41 per cent class III 36 per cent class IV 8 per cent and class V 1 per cent giving an Arneth Index of 73 and a weighted mean of 2.4. If no shift to the left be claimed until the Arneth Index exceeds the extreme limit of the European mean of 58 the following results were found — 18 per cent of the Africans had no shift to the left (Arneth Index below 65) 17 per cent had a very slight shift (A.I. 65-70) 40 per cent had a moderate shift (A.I. 70-80) and 25 per cent had a marked shift (A.I. over 80). The shift to the left in the Africans was chiefly due to a marked increase in the cells of class II, namely the newly segmented neutrophils of the peripheral blood. F. Vargabroyd

BERT E. A. Sickle Cell Disease in the Balovale District of Northern Rhodesia.  
*East African Med. J.* 1946 Mar. 23 No. 3 75-88 1 map

Using vaseline-sealed cover-glass preparations of capillary blood examined at intervals up to 48 hours the author found that the overall incidence of the sickle cell trait in 815 consecutive in-patients of the Government Hospital at Balovale an isolated rural area of Northern Rhodesia, was 12.9 per cent. The incidence among males being 12.5 per cent and among females 13.3 per cent. The incidence of the condition among children that is among those under approximately five years of age was 17.6 per cent whereas for those above this age the incidence was only 12.1 per cent. A few patients were examined for sickling in vivo but the condition was not so demonstrated. Some were also examined for the trait by the method of sealing citrated blood under paraffin in test tubes with fixation of the cells by the addition of formalin at the end of 48 hours to obtain the best results it was found that the citrate solution should be boiled before use in order to expel all air.

It was difficult to assess the amount of anaemia due to sickle cell disease as 48.7 per cent of the population harboured hookworms 22 per cent *S. haematobium*, 2.5 per cent *S. mansoni* while in addition at the height of the rains in February 92 per cent of the children under five years of age had malaria parasites. The incidence of helminthiasis was the same among patients with or without the sickle cell trait but it was found that when the transmission of malaria was at its lowest the parasite rate for sicklers was considerably less.

than for the non sicklers whereas the rates were approximately equal for sicklers and non-sicklers at the height of the rains when malaria was most prevalent.

The familial character of the sickling cell phenomenon was confirmed as the incidence of the trait among the offspring of a group of 33 affected parents was 65 per cent but there was no evidence that the trait was sex linked.

The Balovale District can be divided into seven areas and study of the incidence of the sickle cell trait in these and adjacent areas suggests that there have been little if any movements of populations within the District from east to west during recent years that there has been considerable emigration of Portuguese natives into the land east of the Zambesi River but little into the land west of the River and that the amount of emigration of Northern Rhodesian Lovale resident west of the River over to the east bank has been small compared with that from the north by the Portuguese Lovale into the same part of the District. This last conclusion is unexpected although the others are more or less borne out by what is known of the history of the District. No detailed investigation of the origin of the Lovale now residing east of the Zambesi has ever been made however and in view of the haematological findings it is suggested that an investigation of this nature should be undertaken since definite information on the point would have administrative value.

F Murgatroyd

## VENOMS AND ANTIVENENES

SOBRINHO O P. Anaveneno e o seu valor na produção de soros anti  
ofídicos [Anavenene for preparing Antisera against Snake Venoms.]  
*Arquivos do Inst. Químico-Biol. Estado e Minas Gerais* 1945 v. 1 27-32  
English summary (5 lines)

In 1936 the method of production of antivenenes was to prepare a stock venene consisting of venom 10 gm. glycerin 80 cc. normal saline 120 cc. For stock *Bothrops* venom a mixture was made of *B. jararaca* 8 gm. and 1 gm. of each of *B. alternata*, *B. beuensis*, *B. atrox* and *B. jararacussu* in 0.75 per cent saline and fragments of camphor were added to preserve it. This was left at room temperature for a month with daily shaking. It was then injected subcutaneously twice weekly into horses starting with a dose of 0.075 mgm. and by the 25th injection the dose had reached 350 mgm. the total period of immunization was about three months. To obtain a more potent serum 13 more injections were made till at the 38th a dose of 1 000 mgm. was injected.

Another method has more recently been put into operation viz the use of anavenene. For preparing this 13.33 gm. of the venom are triturated with 333.33 cc glycerin 13.33 cc formol and saline to make a litre the mixture is placed in a thermostat at 37°C for 40 days and then filtered. Horses were inoculated subcutaneously with this 42 injections in 245 days starting with 0.005 mgm. and increasing gradually to 0.450 mgm. The first 14 injections were given every four days after that once a week. The serum so obtained was very satisfactory neutralizing 1.5 mgm. of the venom [per cc. ?]. Later still using a preparation containing 10 gm. of venom, 330 cc. glycerin and 10 cc. formol the period of immunization was reduced by eight weeks. One great drawback to this method is the frequency with which abscesses follow inoculations but these are in most instances sterile which is not the case when venom itself is used.

H Harold Scott

- MARTINS A V. Sobre o uso do anaveneno na produção do soro anti-escorpionico. [Anavenene in the Production of Scorpion Antivenene.] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais* 1945 v 1 7-18 [10 refs.] English summary.

VAGALLES in 1908 prepared a serum against scorpion venom by injecting intravenously into oxen increasing doses of scorpion venom and using camondongos as his test animals. The author has modified this method in each particular. He uses the horse instead of the ox, the anavenene in place of the venom, subcutaneous inoculation in place of intravenous, and guineapigs instead of camondongos. His objections to the ox are that the amount of serum obtained is less than that from the horse, that ox-serum is relatively toxic to some laboratory animals and to man, that there is a risk of anaphylaxis to those sensitized to beef protein, and, lastly, the horse is a more docile animal for these injections. The use of anavenene is preferable to venom because its toxicity is much reduced while its antigenic potency is retained. Guineapigs are easier to rear and to maintain than are camondongos.

The horses were inoculated every 6-7 days with increasing doses of the anavenene of *Tityus serrulatus* and tests were made after the 8th-9th injections, others after the 7th and 15th.

The author claims, and his protocols support the claim, that by his method he obtains much larger amounts of antivenene which moreover has greater antitoxic potency and is produced in less time than by the older mode of procedure.

H. Harold Scott

- MARTINS A V. Anaveneno escorpionico [Scorpion Antivenene.] *Arquivos do Inst. Químico-Biol. Estado de Minas Gerais* 1945 v 1 19-26. English summary (5 lines).

The preparation of scorpion antivenene by repeated injection of the venom into animals has several drawbacks. The author consequently tried using the anatoron (anavenene) to determine whether it would prove as useful in preparing scorpion antivenene as the corresponding product had proved serviceable for snake antivenenes. He found that by addition of toluol in gradual quantities to form a layer some 5 mm. thick over the venom contained in dark-coloured vials and kept at 4°C. the venom could be preserved for several months without loss of toxicity. If kept at 37°C. its toxicity was reduced to one-sixth in six weeks.

He next found that addition of 1 per cent. formal to the venom and maintaining the mixture at 4°C. reduced the toxicity to about one-tenth without affecting its antigenicity.

H. Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES

- GOLDBERG L. C. An Unusual Lichenoid Dermatitis. *J. Amer. Med. Ass.* 1946 Mar 23 v 130 No 12 775-80 10 figs.

This is another report concerning the lichen planus-eczematoid dermatitis complex which has been described on several occasions in American literature, and which has received attention in the British medical press [see this *Bulletin* 1946, v 43 148, 301, 478].

Except in regard to therapy Goldberg has little new information to add. His observations are based upon a large number of patients returned, because

of this malady to the United States from the South Pacific Theatre of Operations and geographically similar areas. Like other authors he describes phases of dermatitis exfoliative dermatitis and lichenoid eruptions which may occur during the course of the disease. He states that he has never seen a classical lichen planus papule with Wickham's striae in an original case although such lesions have been seen in three relapsing cases. The typical lesion of the lichenoid phase is similar to that occurring in hypertrophic lichen planus rather than to the polygonal umbilicated papulo-squamous lesion described by Erasmus Wilson. Goldberg records that the lichenoid papules are often present on the face especially the eyelids and ears, and he describes an appearance similar to erythema ab igne which may be noted on the eyelids when the eruption subsides. In 12 out of 60 cases studied the mucosae of the mouth lips penis or vulva were involved and in 3 out of 20 patients examined proctoscopically greyish white mucosal alteration was seen in the rectum on the columns of Morgagni the crypts not being involved. Gastroscopy failed to reveal lesions on the gastric mucosa. In a discussion of the aetiology Goldberg states that he has been unable to reproduce the lesions by the administration of atabrine mepacrine in the cases observed. All these [patients] were maintained on suppressive atabrine therapy while they were being treated and in no instance did any new lesions appear while under observation. It is true however that some of the hypertrophic lesions would weep but this could readily have been a reaction to local treatment. Several patients developed their first attacks of malaria or relapsed while in this hospital and were treated with intensive atabrine therapy but there was no aggravation of their skin lesions. One patient in particular with severe exfoliating dermatitis plus his lichenoid lesions has been observed for eight months during which time he has been receiving continuous suppressive atabrine therapy he has recovered except for scattered sepia brown pigmentation. Patch and intradermal tests with atabrine were done in a few of these patients and all were found to be negative. No passive transfer tests were made. Although atabrine may be a definite causal factor or an agent that prepares the soil more evidence will have to be uncovered before it can be pinned down as the exclusive and certain etiologic factor. Goldberg suggests that the neurophysiologic mechanism photosensitivity and infection appear to play roles as may as yet unknown geographic factors. He could not reach any definite conclusions as to a possible nutritional factor in producing this dermatosis.

In the treatment of the dermatitis phase the mildest salves and lotions could be used for the skin was easily irritated. Exfoliating cases were treated by the usual methods employed in any exfoliating dermatitis such as continuous wet dressing with 1/5000 potassium permanganate solution, corn starch and baking soda baths high caloric diets with added vitamin medication and the intramuscular administration of crude liver extracts in doses of 2 to 5 cc every day or on alternate days amino acids were given orally in large amounts. In the lichenoid phase small doses of oxophenarsine hydrochloride ['Alapharsen'] were given 0.02 gm bi weekly many of the patients responded well and the pruritus was often relieved before the third injection. The lesions of the mucosae responded equally with those on the skin. In no case were more than ten injections required to cause involution of the lesions. Several of the patients treated with Alapharsen developed fever up to 102°F about six hours after the first injection and when this happened administration of the drug was discontinued. It was believed that these cases had a subthreshold hepatitis which might have been caused by atabrine and activated by the arsenical injection, for their icteric indices were raised and some developed clinical jaundice. The reactions subsided in 48-72 hours

[August, 1948]

(2) Factors which reduce the liability of a person to prickly heat are (a) age below thirty years, (b) previous sun tan (c) loose clothing, (d) open-air working and sleeping (e) low temperatures of place of work, and (f) perhaps the fact of belonging to blood group A (11)

(3) Factors having no effect on the incidence of prickly heat are (a) weight (b) sweat reaction (c) wearing of open-necked shirts, and (d) the effects of the sun on the subject's skin.

(4) Factors which from our investigations gave inconclusive results were (a) type of work, (b) humidity (c) brand of soap used.

These various factors do not seem to be a cause in themselves, but when present they affect a susceptible person as indicated. The disease seems to be more constitutional than to be due to any one factor in particular

[Besides the observations summarized above the paper contains some clinical notes on the diagnosis and treatment of the conditions.]

R. M. B. MACHARUNA

## TROPICAL ULCER.

SHEPHERD Margaret M. Metastatic Osteomyelitis Secondary to Tropical Ulcer. *Brit. J. Surgery* 1948 Apr v 33 No 132 352-7 5 figs.

Id 11 out of 88 cases of tropical ulcer of the leg in young Gurkha soldiers, treated in hospital in Dehra Dun in the latter part of 1943 inflammatory lesions developed in various long bones the tibia was affected in six cases the femur in 3 the fibula in one, the radius in one and the clavicle was also involved in a patient in whom both tibiae were affected. The author has since seen two cases where the lesions were in the shaft of the humerus.

The first symptom was local pain and tenderness not usually severe and not usually complained of for several days after its onset in seven cases there was slight fever. The time of onset of this complication was usually several weeks—4 to 27—after the ulcer appeared and the ulcer was then clean and healing except in one case.

Radiologically the first change was a decalcification in the cortex of the diaphysis of a long bone. Then followed linear periosteal new bone deposit and a fluffy or woolly new bone having a broadly crenated outline. In some cases healing then occurred by deposition of calcium salts in the new bone. Very little resorption took place. In other cases changes indicative of osteomyelitis appeared before healing took place. The bone lesions are clearly shown in the radiographic illustrations.

Wassermann and Kahn tests were asked for and reports were received in nine cases but in one the blood was haemolyzed and in another it was contaminated the other seven were negative.

The bone lesions healed without special treatment (sulphathiazole was given in four cases) in from 5 to 27 weeks, average 12 weeks. In a footnote the author states that penicillin was tried in a few other similar cases with encouraging results.

[No bacteriological examinations appear to have been made except that in one case it is stated that blood culture was sterile.] J. F. CORSON.

MANOWA, S. L. A. An Excision Knife for Tropical Ulcers. *Brit. Med. J.* 1948 Apr 13 874 1 fig.

This knife is a bistoury curved on the flat. The author has found it useful for the excision of tropical ulcers.

## MISCELLANEOUS DISEASES

CULLINAN E. R. Medical Disorders in East Africa: *Trans Roy Soc Trop Med & Hyg* 1946 Apr 1 39 No 5 353-68 1 map [11 refs] Discussion 368-72 [KEKWICK A. WILCOCKS C. MANSON BAHR P. BIGGAM A. G. BOYD J. S. K. JAMES S. P. LOW G. C. McCULLAGH Mch. NAPIER, L. E. CULLINAN E. R. (in reply)]

This paper briefly surveys the medical disorders affecting British troops in the East Africa Command during the last 20 months of the recent war and makes a plea for future co-ordinated clinical research in East Africa.

The East Africa Command covered over a million square miles extending from 11°N to 25°S. It included Kenya Tanganyika, Northern Rhodesia, Nyasaland Italian and British Somaliland and the reserved area of Abyssinia, Madagascar Mauritius the Seychelles and Zanzibar. The troops were fairly static at the time being in training for service in South East Asia and they comprised a cross-section of the fittest young adult native males of East Africa, and a representative sample of adult Europeans, all living under closely similar conditions.

The most prevalent medical causes of admission to Hospital, in both Europeans and non Europeans were malaria, dysentery and enteritis (including amoebiasis) and then upper respiratory infections. The incidence of other diseases however differed markedly in the two groups dengue and typhus being found mostly among Europeans while schistosomiasis relapsing fever leprosy and yaws were almost exclusively confined to the non Europeans. Digestive disorders were nearly five times skin diseases over three times and psychoneurosis over twice as frequent among the Europeans as among the Africans. The killing diseases of the Africans were tuberculosis meningitis and pneumonia, accounting respectively in 1944 for 16.0 per cent 12.1 per cent and 11.7 per cent. of all non-European deaths.

Nearly all the malaria in the mainland was due to *P. falciparum* but in a few districts especially in Somaliland Madagascar and Mauritius *P. vivax* was found while in Mauritius and rarely elsewhere *P. malariae* occurred. The malaria season varied greatly from region to region, but in the hyperendemic areas transmission was almost perennial. Immunity was labile depending upon the frequency of infection, and while the disease among non-immunes was of all grades of severity it was almost universally mild among the immune populations. It was therefore neither desirable nor necessary to give an immune African a full course of treatment for malaria.

Bacillary dysentery ran a mild course with few exceptions and the case-mortality was low: the deaths nearly all resulted from dehydration which seemed to occur more rapidly among the Africans. In the treatment of the disease sulphapyridine seemed as effective as sulphaguanidine.

The incidence of amoebiasis rose among Europeans as the years of war went by and in 1944 the number of European troops admitted to hospital with the disease corresponded to 20.27 per 1000. Treatment followed conventional lines with the usual rapid resolution of symptoms but in many of the European patients the disease relapsed, and those with frequent recurrences were generally sent home to the United Kingdom.

Skin diseases were relatively uncommon in African troops and among Europeans they were frequent only in humid stations. Tropical ulcers were very prevalent among the African troops in the earlier part of the war but towards the end of the war had almost completely disappeared.



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Psychoneurosis accounted for 17.50 per 1,000 of the admissions of the European troops to hospital an incidence rate not unduly high in view of the prolonged absence from home loneliness and lack of action. The majority of the European patients suffered from anxiety states whereas hysteria was the common condition among the Africans.

Relapsing fever common in many parts of East Africa, was largely confined to the native population. It appeared to be tick-borne except in Abyssinia, where the louse-borne type was also found. Ornithosis, cerebral complications appeared more frequently than among the Europeans, whereas where the tick vector responsible for the disease occurred in Africans. Ornithosis, although penicillin had some effect the results were not sufficiently good to justify its general use.

The incidence of schistosomiasis among Europeans was very small. The few Africans admitted to hospital with the condition gave no real measure of the true incidence of the infestation among the natives, as an examination of the urine of 1,468 African troops all of whom were in actual training and apparently fit revealed that 13.58 per cent were harbouring eggs of *S. haematobium*. The highest percentage of infected men came from Vassaland, where there is a large lake whose surrounding population is considered by local observers to be heavily infected from early childhood, the infection rate being estimated at 80 per cent of the inhabitants. Rectal schistosomiasis appeared to be relatively uncommon, and the incidence of *S. mansoni* throughout East Africa is not accurately known.

Acute pyogenic meningitis was much commoner in African than in European troops, and had a very severe clinical course usually the infection was meningococcal, but sometimes it was pneumococcal, no other local focus being found, and these pneumococcal infections were often particularly resistant to treatment both with sulphonamides and with penicillin.

Dengue was particularly common in Diego Suarez at the northern extremity of Madagascar, and 84.2 per cent of all the cases in the Command occurred there during the first five months of 1944. Europeans were attacked over eight times as frequently as Africans. There were remarkable similarities between the clinical features of the disease and those of sandfly fever. There were a few small scattered outbreaks of idiopathic infective hepatitis the course of this disease was no more severe in Africans than in Europeans and the incidence was much less, while the opposite was true of post-erythema-tic jaundice. Africans being more frequently and more severely affected than Europeans. Acute anterior poliomyelitis was rare excepting for a violent outbreak among the children in Mauritius early in 1945 when 1,000 cases occurred in a population of approximately 450,000. Leprosy was not uncommon among African troops, and was almost always of the neural type. Although malnutrition was frequent in recruits from Diego Suarez, whose diet for a time had consisted mainly of a sharp outbreak of nutritional deficiency among some East African troops stationed in Diego Suarez, whose diet for a time had consisted mainly of rice. This rice had been lightly milled, and in its uncooked state contained a theoretical sufficiency of thiamin. It was found, however, that while fresh lightly milled rice lost only 30 per cent and, moreover, it produced beriberi in pigeons. Generally acute and frequently ran a severe course with a high death rate. There is, however, a group with higher resistance which responds well to treatment but unfortunately most of the patients are unwilling to stay in

hospital for longer than three months. The African refuses to be separated from his family and one possible answer to the problem is the "settlement system" a tuberculosis centre on the lower slopes of Mt. Kilimanjaro in Tanganyika is already doing excellent work in this direction.

The author stressed the need for co-ordinated epidemiological and clinical research in the Colonial Empire in the future not only for its potential scientific value but also for the interest it could give to large numbers of medical officers in remote stations. In June 1944 the D.D.M.S. inaugurated a Medical Investigation Committee for the purpose of encouraging facilitating and correlating research by medical officers in the East African Command. The response was immediate and enthusiastic, and within a year a considerable amount of valuable work had been done.

In the subsequent discussion several speakers enlarged on the desirability of further and wider research in the tropics. Brigadier J. S. K. Boyd mentioned that a Colonial Medical Research Committee had been formed to foster research on a wide basis with whole-time research workers. C. WILCOCKS thought that tuberculosis in the tropics demanded more attention and stressed the importance of poverty and ignorance in the aetiology of this and many other diseases in the tropics. Colonel S. P. JAMES was surprised to hear that nearly all the malaria had been due to *P. falciparum* and suggested that other species of parasite were not without importance in East Africa. Dr G. CARMICHAEL Low stated that the diseases reviewed were much as he had seen them in East Africa more than 40 years ago excepting that infection with *S. mansoni* was then common as were other helminthic infestations particularly filarial. Mr McKIM McCULLOCH remarked on the preponderance of appendicitis in Europeans as compared with Africans.

F. Murgatroid

AVERY J. L. Parasitic Infections among Natives of the Samarai District, Papua, New Guinea. *J. Parasitology* 1946 Feb v 32 No 1 25-9

Stained thick blood films and faecal specimens (one of each from each person) of natives in New Guinea were examined for parasites the faecal examination included a brine floatation method. One survey was made of a group of labourers chiefly to ascertain filarial periodicity while another survey was made of an entire native village adults and children [only three children aged 0-4 years had a blood examination in this village of 318 persons examined all three had malarial parasites].

The following incidence of infection was found in the village. *P. vivax* 105 *P. malariae* 50 *P. falciparum* 7 *Wuchereria bancrofti* 97 (taken at 9 p.m. to midnight). No mepracine was given to the natives except in the rare cases where seriously ill persons were taken to hospital. The microfilariae showed definite periodicity, increasing in the peripheral blood at night.

The incidence of *Entamoeba histolytica* was low—3 out of 53 labourers and 3 out of 300 villagers. Other protozoa found were *E. coli*, *Endolimax nana*, *Giardia lamblia* [*G. intestinalis*] and *Trichomonas hominis* and all had a low incidence (1 or 2 per cent.).

Two species of intestinal helminths were found. *Trichuris trichiura* (1 out of 53 labourers and 126 out of 300 villagers) and hookworms (40 out of 53 labourers and 263 out of 300 villagers) the species of hookworm could not be determined.

*Anopheles punctulatus punctulatus* was very abundant other mosquitoes present were *A. p. moluccensis* [*A. p. farauti*] *Aedes scutellaris* and *Aedes kochi*.

LINDSAY S F Fatigue Syndromes in West Africa. *Brit Med J* 1946  
May 18 758-60

A number of men of the British Army in West Africa Command who showed signs of physical and mental fatigue were studied from the point of the relation of climate to ill-health in the moist tropics.

The cases 88 in number were classified into five groups, the first consisting of 84 with fatigue as the main symptom. This group was sub-divided into (1) those with signs of simple physical and mental fatigue (2) those with exaggerated or abnormal psychological reactions, (3) those with toxic illness. The remaining groups consisted of those with psychoneurosis, depressive states, psychosis and a post-concussion syndrome complicated by fatigue symptoms.

Investigation showed that the West African climate was only partly the cause of the breakdown. Everyone living in this climate is liable to experience some degree of languor but most people learn to adapt themselves to the limitations thus put upon their activities. The part played by the climate is to aggravate any pre-existing weakness physical or psychological. Even the problem of adjusting themselves to the ways of the African native is too difficult for some people and they react with irritability and frustration, leading to tiredness and depression.

The total personality with its physical, intellectual, emotional, social and moral components must be considered when studying reactions to climatic stress.

Some detailed case histories are given.

[An interesting study of fatigue problems in an unusual setting providing some further confirmation of previous findings in various industrial environments particularly noticeable owing to the exaggerated conditions resulting from the war]

May Smith

DOWLING P G Epidemic Polyarthritits. *Med J Australia* 1946 Feb 23  
v 1 No 8, 245-6

This is a description of an outbreak of a short, mild fever accompanied by polyarthritits, which occurred among Australian troops in North Queensland during February, March and April, 1945. The disease was obviously the same as the "acute polyarthritits" described by HALLIDAY and HORAN as occurring in the Northern Territory of Australia [see this *Bulletin* 1944 v 41 279]. An outbreak in Queensland in 1944 was described by SIMON.

In the present outbreak 94 cases occurred among various units in a camp seven miles in length. In a unit at one end of the camp there were 47 cases. In four units a short distance away there were 39 cases. The remaining eight cases were from units in other parts of the camp.

Every patient suffered from pain and stiffness of several joints especially those of the hands and feet. Swelling was observed in about three-fourths of the cases, and there was effusion into one knee-joint in three cases.

The swelling which was periarthritic in most instances, persisted for four to seven days. The pain usually disappeared a few days later but in three cases it lasted for three months. Some of the patients had no fever but most of them had a slight rise of temperature to 99-101°F for two to five days. One patient exceptionally had a temperature of 103°F. The onset was gradual. In 90 per cent. of the cases there was a papular or macular rash, which appeared on the first to the seventh day and lasted for two to seven days. It was usually first seen on the trunk, then on the limbs. Sometimes it was generalized.

In four cases small vesicles developed on the papules within twenty-four hours of the appearance of the rash, and these patients were first thought to

be suffering from varicella. Redness of the fauces was seen in 12 patients. One or more groups of lymph glands were swollen and tender in about half of the cases.

The leucocyte picture was normal. Blood cultures were sterile. The outbreak, like the others recorded occurred in the wet season it began two weeks after heavy falls of rain and was associated with a great increase in the prevalence of mosquitoes. Two weeks after the commencement of the outbreak and one week after starting mosquito-control measures new admissions rapidly diminished in numbers.

*Culex fatigans* was the only mosquito of which adults were found in all the three camps in which a survey was made. It was present in large numbers. Larval *Aedes notoscriptus* and *Aedes albopictus* were found. Adult *Anopheles annulipes* were found in two of the camps and adult *Culex lutzii* in one. Other possible insect vectors were considered, but none was prevalent in the area at the time. There was no evidence of spread by contact, and the author concludes that the possibility that this disease is a mosquito-borne infection requires investigation.

He suggests that the name epidemic polyarthrititis is suitable for the condition, because it avoids confusion with other serious forms of polyarthrititis.

[The name proposed by the author for this problem fever seems to be preferable to acute polyarthrititis. As opportunities for investigation into the cause may not recur the disease will perhaps remain one of the minor unsolved mysteries of the war. The name polyarthritic febricula would possibly have been more descriptive than the others suggested.] *John W. D. Megaw.*

RUDRA M. N. & BHATTACHARYA, K. P. Serum Phosphatase in Lathyrism. *Lancet* 1946 May 11 633.

Lathyrism is the result of degeneration of part of the nervous system and there is an intimate relationship between vitamin B<sub>1</sub> and the nervous system. The authors therefore studied the nutrition of lathyrism patients from this vitamin aspect but found that the vitamin was present in normal limits in the blood and urine. They next estimated the serum-phosphatase in normal subjects and compared it with that of sufferers from lathyrism. In 12 of the former it ranged between 0.8 and 5.7 units with a mean of 2.38; among 10 lathyrism cases it ranged between 18.7 and 56.5 with a mean of 38.7 units. It is suggested that this increase may destroy the circulating co-carboxylase so that the patient is functionally though not actually deficient in vitamin B<sub>1</sub> with consequent affection of the nervous system.

This is put forward as a hypothesis but the hiatuses to be filled are great. The authors can offer no explanation of the increase of serum phosphatase in lathyrism and themselves make the suggestion that it may not be the cause but the effect of lathyrism for usually the serum phosphatase level is a measure of the severity of the disease. [A stimulating piece of work.]

*H. Harold Scott.*

## GENERAL PROTOZOOLOGY

LEHMANN, G. D. & PRENDIVILLE, J. T. Occurrence of a Flagellate in the Sputum of a Case of Bronchiectasis. *Brit Med J* 1946 Feb 2, 158-60. 2 diagrams. [17 refs.]

The paper describes a case of bronchiectasis in which flagellates in diminishing numbers were present in the sputum on four successive days. The disappearance of the flagellate coincided with the relief of symptoms under sulphyridine treatment which however did not prevent a fatal issue. The

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flagellate 10-15 $\mu$  in length by 5-7 $\mu$  in breadth was actively motile its movements being the result of the action of two equal anterior flagella and of amoeboid changes in shape. It was generally pear shaped, the posterior broader end frequently being elongated to form a caudal process. In some respects the organism resembles the flagellate stage of *Dimastigomoea gruberi* but this organism does not develop an elongated caudal process in its flagellate stage which is merely transitory the stable form being an amoeba. It is suggested that an amoeboid phase might have been present in the lung cavities and that the flagellate phase occurred only when dilution of the material with bronchial secretion and saliva took place. It seems not unlikely that the organism is an altered trichomonas a possibility considered by the authors. No pathological significance is attributed to the presence of the flagellate in the material coughed up from the lung. The paper is illustrated by a number of line drawings.

C M Wenyon

CHIFFAUX C & CHIFFAUX MATHIS Jeanne Le *Trichomonas vaginalis* chez la femme noire togolaise. Etude épidémiologique clinique pathogénique et thérapeutique. *IT vaginalis* in Togoland Women. *Médecine Tropicales*. 1944 Sept-Oct.-Nov.-Dec. 4 No 4 289-300 [21 refs.]

The authors have examined 151 native women of Togoland, aged 18 to 45 for evidence of *Trichomonas vaginalis* infection which might account for the symptoms of pain and vaginitis of which they complained. Of these women 45 were found infected giving an incidence of 29.8 per cent. which is nearly double the infection rate encountered among white women making similar complaints examined in Marseilles. The authors think that the higher incidence amongst the black women may be due to some particular racial susceptibility. They admit that *T. vaginalis* is usually present as a saprophytic organism only but that occasionally it may take on pathogenic properties. The paper discusses main aspects of the subject the authors basing their remarks on personal observations and a general review of the literature.

C M Wenyon

## GENERAL ENTOMOLOGY

JUNTER G W WELLS, T H & JAMES, W G Jr An Outline for teaching Mosquito Stomach and Salivary Gland Dissection. *Amer J Trop Med* 1946 Mar v 29 No 2 221-8 13 figs. [17 refs.]

The technique of mosquito dissection described in this paper is not new neither is the method of teaching it but after trying many others they were adopted by the American Army Medical School as being the most satisfactory for the training of large groups of individuals who had no previous knowledge of entomology.

The course consists of one lecture on mosquito anatomy followed by two practical periods of two hours each. Uninfected mosquitoes are dissected during the first practical period and infected ones during the second. A full description of the technique is given, oöcysts and sporozoites are described and illustrated and there is a list of the necessary equipment. A useful paper for the beginner.

H S Lacey

SAUTET J & AUDIBERT Y Etudes biologiques et morphologiques sur certaines larves de moustiques en vue d'applications pratiques pour leur destruction. (Première partie.) [Biological and Morphological Studies on Mosquito Larvae.] Bull Soc Path Exot. 1946 v. 39 Nos. 1/2 43-61 13 figs

The work described in this paper was done at the Hygiene Research Centre, Marseilles where the mosquitoes *Theobaldia longiareolata* *Culex pipiens* and *Culex hortensis* are being studied.

An account of the structure and function of the terminal respiratory apparatus of the larva of *Culex pipiens* is followed by a description of some experiments on larvae imprisoned under water. Survival times of such larvae were recorded at different instars in standing and running water under winter spring and summer conditions in the presence and absence of aquatic vegetation and food. Usually six to eight larvae were put into two litres of water.

Some of the results are tabulated and briefly discussed, and in general tend to show that submerged larvae are able to withstand such conditions for longer periods in water which is cold and running than in warm still water the presence of food and aquatic vegetation helps to prolong their resistance. First and second stage larvae are shown to be more resistant to mechanical suffocation than are the older larvae.

The paper is to be continued.

H S Leeson

SIMMONS S W & Staff Techniques and Apparatus used in Experimental Studies on DDT as an Insecticide for Mosquitoes. Supplement No 189 to Pub Health Rep Wash. 1945 3-20 11 figs

Important outstanding problems in mosquito control by DDT are the number of mosquitoes leaving treated houses before having received a lethal dose of insecticide and the relation between lethal effect and dosage and interval since application on different wall surfaces. The authors describe techniques used in investigating these subjects. This review merely indicates the general scope of their equipment which is described in the original in sufficient detail to make exact reproduction possible.

Mortality amongst mosquitoes leaving treated houses is studied by means of a window trap placed over windows on northern or western aspects of the house. Several types have been tried in the most successful type some windows and doors were left open to allow free ingress of mosquitoes and one or two windows are closed by means of a framework, in the general shape of a window hinged at the bottom and opening outwards to an angle of about 15 degrees from the vertical. The upper horizontal surface of this frame has an opening over which a cage is placed and left for 24 hours this is subsequently removed and used as a holding cage in which mosquitoes can be observed without further handling. A bigger catch is obtained by this means than by others which have controlled inlets as well as outlets and specimens captured are considered to be a representative sample of those leaving the room by all apertures.

Testing of toxicity of surfaces may be needed under two sets of conditions (1) in rooms which have been treated and occupied in a normal manner and (2) in the laboratory where it is desired to remove all disturbing factors such as mechanical handling so that the treated surface can be left under standardized conditions. For the first of these the authors use a holding cage in the shape of a truncated cone and made of plastic a plunger cage resembling an enlarged syringe by means of which mosquitoes can be transferred with the minimum of trauma and glass Petri dishes held in a special framework attached to the wall

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by means of brackets 15 to 20 mosquitoes being held between the Petri dish and the wall and preferring to alight on the latter as a result of their difficulty of holding on to the glass. After exposure to the treated surface, mosquitoes are liberated into holding cages for observation.

For laboratory tests the authors use a darkened holding cage a glass lantern chimney which mosquitoes are persuaded to enter by light attraction, an air blast mechanism by which they are transferred without damage to the experimental cage arranged to accommodate panels of wood or other material which have been treated under standardized conditions. At the end of the exposure time mosquitoes are transferred to observation cages.

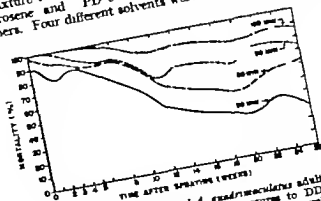
[These last two techniques provide a rapid method of accurately estimating the toxicity of surfaces to mosquitoes artificially held in contact with them which should yield results which can safely be used in statistical comparisons. The same degree of reliability could not be attributed to the first technique for the estimation of mortality amongst mosquitoes entering treated rooms.]

G Macdonald.

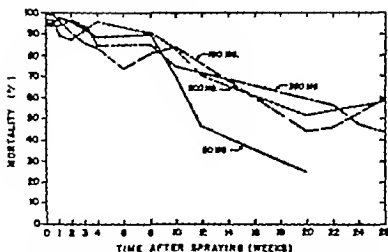
FAY R. W. SMOOKS S. W. & CLAPP J. M. Laboratory Investigations on the Toxicity of DDT Residues to Adults of *Anopheles quadrimaculatus* Supplement No 186 to Pub Health Rep Wash 1945 21-34 11 figs.

Using the technique described by SMOOKS and Staff (see above) *Anopheles quadrimaculatus* mosquitoes of both sexes as test insects doses of DDT of 50 100 200 and 300 mgm. per sq. ft. exposure periods varying from 35 to 120 minutes and periods of observation up to 26 weeks the authors show that mortality varies directly with exposure time but not materially with the dose of DDT applied, provided it is 100 mgm. per sq. ft. or more. In fresh films the effect of variations in the period of exposure of mosquitoes is relatively slight but in older films it increases until in films 26 weeks old there is a mortality of 31.2 per cent. amongst mosquitoes held in contact with them for 35 minutes and of 89.1 per cent. amongst those in contact for 120 minutes. These results are illustrated in the two graphs reproduced below.

The residual activity of DDT deposited from different solvents again observed over a period of 26 weeks showed moderate differences. The toxicity of a film deposited from an orthodichlorobenzene mixture wore off rapidly and a Drefl Tak mixture showed poor adhesion and had to be abandoned. Gas condensate kerosene and PD 544 C and PD 544 B appeared to be better than others. Four different solvents were also used for the preparation



Average 48-hour mortalities of 4 *quadrimaculatus* adults after 35- 60 90 and 120-minute exposures to DDT residues of 50 to 300 mg per square foot from 1 to 26 weeks after application



Per cent. mortalities of *A. quadrimaculatus* adults after 80-minute exposures to 50 100 200 and 300 mg DDT per square foot residue at 1 to 28 weeks after application.

[Reproduced from Supplement No 186 to the Public Health Reports]

of films exposed to weathering and no material difference was found between them. In each case direct sunlight produced a slow steady deterioration in effect whilst rain produced a rapid deterioration over the first four weeks after which no further change occurred up to eight weeks.

[The observation that the dose of DDT does not materially affect mortality rates conflicts with the findings of other authors notably METCALF *et al* (this Bulletin 1946 v. 43 102). The range of doses in the two cases was very different 50 to 300 mgm. in the present series 40 to 1 000 in the previous series but they do seem to display some material difference. The exact techniques used in the present series must be considered as making their results very reliable.]

G Macdonald

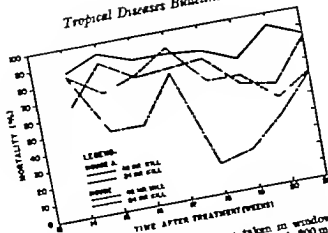
TAREWELL C. M. & STIERLI H. The Evaluation of DDT Residual Sprays for the Control of Anopheline Mosquitoes in Dwellings. Supplement No 186 to Pub Health Rep Wash 1945 35-48 5 figs.

The net mortality of mosquitoes naturally entering unoccupied rooms was studied by the method elaborated by SIMMONS and STAFF [see above] in which a proportion of those attempting to leave are captured and held under observation for 24 or 48 hours. The majority of the mosquitoes were *Anopheles quadrimaculatus* and about 77 per cent of the dead recovered were males. This high proportion is attributed to the fact that the experiment was carried out close to breeding places and possibly to a higher resistance of females than of males to DDT. The mortality figures obtained in treated houses were checked by the findings in untreated control houses and corrected by a formula which took account of the numbers dying naturally in the untreated places. The results in two representative vacant buildings are shown graphically in Figure 1.

When a similar technique was tried in occupied houses the net kill was much lower. For periods of two to six weeks after treatment mortalities of 39 per cent. at 24 hours and 54 per cent. at 48 hours were recorded the reduction being attributed to the presence of furnishings and objects hung on the walls which greatly increased the amount of untreated surface on which mosquitoes might alight. There were indications that doses of 200 to 400 mgm DDT per sq ft were more effective than doses of 100 mgm.



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Effective 24 and 48-hour mortalities taken in window-traps of unoccupied houses A and B, treated with 800 mg of DDT per square foot. Each point is a summation of 7 daily collections.

[Reproduced from Supplement No 188 to the Public Health Reports]

In addition to these trials on mosquitoes naturally entering rooms others were made in which captured or insectary-bred *A. quadrimaculatus* were liberated into rooms all openings from which could be occluded by traps, and which had been treated with 100 200 400 and 800 mgm. DDT per sq ft. Five to 35 minutes after release the mosquitoes became irritated and began to move about some towards the light simultaneously suffering from tremors and incoordinated flight. The number moving towards the light gradually increased till the numbers resting on the untreated screen of the window trap reached a maximum between 30 and 60 minutes after release. Many of those moving towards the light had, however, already received a dose which proved fatal before they actually entered the window traps, and of those which entered them practically all died within 24 hours. (Contrasting recently-applied and ageing films it was found that with the latter the time required for knockdown was increased but that otherwise the results were substantially the same as with the former. Rate of knockdown was also affected by dosage 50 per cent morbidity being reached at 90 67 and 60 minutes after liberation into rooms treated with 100 200 and 800 mgm per sq ft.)

In some of the experiments the temperature was recorded, and it is stated that temperature greatly influenced the rate of knockdown the higher the temperature the more rapid effect of the DDT. In the opinion of the reviewer the data presented are inadequate to substantiate this statement.

G Macdonald

STIERLI H SIMON W TAYLOR C M Operational Procedures and Equipment used in the Practical Application of DDT as a Residual House Spray Supplement No 183 to Pub Health Rep Wash. 1945 49-65 5 figs

ketosene solutions of DDT were found to have practical disadvantages which made the use of emulsions preferable. A formula found useful for large scale work was —DDT 3 lb xylene 3 quarts and Triton X 100 (a proprietary emulsifier) 6 fluid ounces. One gallon of a concentrate made to this formula, mixed with 8 gallons of water makes a nominal 5 per cent. spray of which 1 gallon to 948 sq ft. gives a DDT dosage of 200 mgm per sq ft. In cold weather DDT is not so soluble and the concentrate is therefore weaker

for winter work 2 lb of DDT were dissolved in 1 gallon of xylene with 0.2 quarts of Triton X 100 to form a concentrate of which 1 gallon mixed with 3 gallons of water gives a 5 per cent. emulsion

For small scale projects mixing was carried out in a 55-gallon wooden barrel mounted on rockers like those of a rocking chair and fitted with handles by which it could be shaken by means of this 50 gallons of concentrate could be mixed every hour For work on a larger scale a power mixer was devised and is described in detail.

Both hand-operated and power sprayers were used. The hand sprayer was of the pneumatic type in which before working, an air pressure of 50 lb per sq in is developed by means of a hand pump A nozzle giving a fan shaped spray at a delivery of 0.2 gallon per minute was used and was held 24 to 30 inches from the wall. The power sprayer when adjusted to 60 lb per sq in pressure delivered 0.24 gallon per minute with which delivery 230 sq ft. could be treated every minute Useful data are given on this and accessory equipment needed in practical work on the training of workers the preparation of houses and the technique of spraying

One overseer and two labourers using power equipment mounted on a truck could spray 40 houses per day each averaging 1 750 sq ft. of surface The cost of treating 1 000 sq ft of surface was —materials 35 cents labour 24 cents fuel, lubricants maintenance and repair (by inference) 10 cents total, exclusive of overhead costs 69 cents.

Piston-type atomizing hand sprays were found to be useless and a power operated paint sprayer was unsatisfactory It was estimated that in urban areas a three man crew with a power sprayer was equal to or better than a five-man crew with hand sprayers and that the cost of their equipment was 400 dollars as against 200 dollars for the five men with hand sprayers

G Macdonald

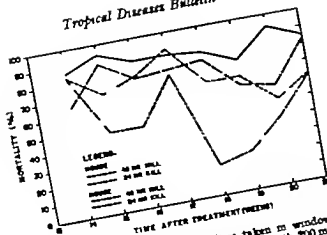
ARNOLD E. H. FERGUSON, F. F. & UPHOLT W. M. The Experimental Use of DDT Sprays as Mosquito Larvicides. Supplement No 186 to Pub Health Rep Wash. 1945 66-79 8 figs

Emulsions of DDT made from concentrates consisting of 5 per cent DDT in oil with various proprietary emulsifier spreaders diluted [? 30 times] with water gave 98 to 99 per cent kill of anopheline and culicine larvae under a variety of conditions when the dose of DDT applied was 0.1 lb per acre There was however a disappointing lack of spread of the DDT from the point of application and experiments showed that the lethal effect was limited to the distribution of the solvent consequently emulsions were considered unsatisfactory for anti larval work. Surface films of non-emulsified oil solutions were superior and a 1.25 per cent. solution of DDT in No. 2 fuel oil with 0.5 per cent B 1956 (a proprietary emulsifier-spreader) was considered satisfactory

A residual larvicidal effect was not obtained with small doses 0.5 lb per acre gave control for only an additional week and had the undesirable effect of killing fish. In one case where 1.7 lb per acre was applied to an area which had previously received 0.9 lb per acre in divided doses the water remained devoid of all animal life except plankton for over a month and samples of the water showed definite toxicity to insectary-reared larvae.

Suspensions of DDT made by adding it to alcohol with a dispersing agent and later diluting the mixture with water had properties similar to those of emulsions. DDT dissolved in heavier than water oil, as a bottom application was inferior to any of the surface applications as a larvicide and was more lethal to other aquatic life

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Effective 24- and 48 hour mortalities taken in window-traps of unoccupied houses A and B, treated with 200 mg of DDT per square foot. Each point is a summation of 7 daily collections.

[Reproduced from Supplement No 188 to the Public Health Reports]

In addition to these trials on mosquitoes naturally entering rooms others were made in which captured or insectary bred *A. quadrimaculatus* were liberated into rooms all openings from which could be occluded by traps and which had been treated with 100 200 400 and 800 mgm. DDT per sq. ft. Five to 35 minutes after release the mosquitoes became irritated and began to move about some towards the light simultaneously suffering from tremors and incoordinated flight. The number moving towards the light gradually increased till the numbers resting on the untreated screen of the window trap reached a maximum between 30 and 60 minutes after release. Many of those moving towards the light had, however, already received a dose which proved fatal before they actually entered the window traps, and of those which entered them practically all died within 24 hours. Contrasting recently applied and ageing films it was found that with the latter the time required for knockdown was increased, but that otherwise the results were substantially the same as with the former. Rate of knockdown was also affected by dosage 50 per cent morbidity being reached at 93 67 and 60 minutes after liberation into rooms treated with 100 200 and 800 mgm per sq. ft.

In some of the experiments the temperature was recorded and it is stated that temperature greatly influenced the rate of knockdown the higher the temperature the more rapid effect of the DDT. [In the opinion of the reviewer the data presented are inadequate to substantiate this statement.]

G Macdonald

STIERLI H SIMMONS S W & TARTWELL C M Operational Procedures and Equipment used in the Practical Application of DDT as a Residual House Spray Supplement No 183 to Pub Health Rep Wash. 1945 49-65 5 figs

Kerosene solutions of DDT were found to have practical disadvantages which made the use of emulsions preferable. A formula found useful for large scale work was —DDT 3 lb. + kerosene 3 quarts and Triton X 100 (a proprietary emulsifier) 6 fluid ounces. One gallon of a concentrate made to this formula, mixed with 6 gallons of water makes a nominal 5 per cent. spray of which 1 gallon to 846 sq. ft. gives a DDT dosage of 200 mgm per sq. ft. In cold weather DDT is not so soluble and the concentrate is therefore weaker

for winter work 2 lb of DDT were dissolved in 1 gallon of xylene with 0.2 quarts of Triton X 100 to form a concentrate of which 1 gallon mixed with gallons of water gives a 5 per cent emulsion.

For small scale projects mixing was carried out in a 55-gallon wooden barrel mounted on rockers like those of a rocking chair and fitted with handles by which it could be shaken by means of this 50 gallons of concentrate could be mixed every hour. For work on a larger scale a power mixer was devised and is described in detail.

Both hand-operated and power sprayers were used. The hand sprayer was of the pneumatic type in which before working an air pressure of 50 lb per sq in. is developed by means of a hand pump. A nozzle giving a fan shaped spray at a delivery of 0.2 gallon per minute was used and was held 24 to 30 inches from the wall. The power sprayer when adjusted to 60 lb per sq in. pressure delivered 0.24 gallon per minute with which delivery 230 sq ft could be treated every minute. Useful data are given on this and accessory equipment needed in practical work on the training of workers the preparation of houses and the technique of spraying.

One overseer and two labourers using power equipment mounted on a truck could spray 40 houses per day each averaging 1750 sq ft of surface. The cost of treating 1000 sq ft of surface was —materials 35 cents labour 24 cents fuel lubricants maintenance and repair (by inference) 10 cents total exclusive of overhead costs 69 cents. Piston-type atomizing hand sprays were found to be useless and a power operated paint sprayer was unsatisfactory. It was estimated that in urban areas a three man crew with a power sprayer was equal to or better than a five man crew with hand sprayers and that the cost of their equipment was 400 dollars as against 200 dollars for the five men with hand sprayers.

G Macdonald

ARNOLD E. H. FERGUSON, F. F. & UPHOLT, W. M. The Experimental Use of DDT Sprays as Mosquito Larvicides. *Health Rep* Wash. 1945 68-79 8 figs. Supplement No 186 to Pub

Emulsions of DDT made from concentrates consisting of 5 per cent DDT in oil with various proprietary emulsifier spreaders diluted (? 30 times) with water gave 98 to 99 per cent kill of anopheline and culicine larvae under a variety of conditions when the dose of DDT applied was 0.1 lb. per acre. There was however a disappointing lack of spread of the DDT from the point of application and experiments showed that the lethal effect was limited to the distribution of the solvent. Consequently emulsions were considered unsatisfactory for anti larval work. Surface films of non-emulsified oil solutions were superior and a 1.25 per cent. solution of DDT in No. 2 fuel oil with 0.5 per cent. B 1936 (a proprietary emulsifier spreader) was considered satisfactory.

A residual larvicidal effect was not obtained with small doses 0.5 lb per acre gave control for only an additional week and had the undesirable effect of killing fish. In one case where 1.7 lb per acre was applied to an area which had previously received 0.9 lb per acre in divided doses the water remained devoid of all animal life except plankton for over a month and samples of the water showed definite toxicity to insectary reared larvae. Suspensions of DDT made by adding it to alcohol with a dispersing agent and later diluting the mixture with water had properties similar to those of emulsions. DDT dissolved in heavier than water oil as a bottom application was inferior to any of the surface applications as a larvicide and was more lethal to other aquatic life.

An enquiry into the reason for the absence of residual larvicidal action showed that the bottom mud complex in some way binds the DDT in a form that is not available to larvae though colorimetric estimation suggests that it is chemically unchanged. 100 gm. of mud will absorb as much as 4 mgm. of DDT in this way and the effect is not dependent on bacterial action.

An experiment with minimal doses of DDT in fuel oil and in gas condensate liquor both of which produce surface films showed that the latter was considerably the better vehicle though with normal doses of 0.1 lb. per acre the two were equal in value.

G Macdonald.

LACKEY J B & STEINLE Mary L. Effects of DDT upon some Aquatic Organisms, other than Insect Larvae. Supplement No 186 to Pub Health Rep Wash. 1945 80-89

DDT applied in a variety of vehicles with different emulsifiers has no effect on macroscopic vegetation though it might be inactivated by the zoogeal coverings of plant stems. Doses of 1.0 part per million are poisonous to *Gambusia affinis* which, however avoids the treated area if there is a safe retreat and thus may escape destruction. Water treated with this amount of DDT becomes non-toxic within 5 days of treatment. Tadpoles and crayfish are killed by similar doses though with the latter the results are inconsistent. Aquatic worms and rotifers are not affected by doses of 0.25 to 1.0 part per million. *Daphnia* and perhaps other crustacea are killed in the laboratory by doses of 0.1 part per million though *Clamvoluta* resist 20.0 parts per million. The evidence indicates that DDT as normally used is harmless to much, if not all of the protozoal and algal population.

The authors suggest that the use of DDT might break the biological chain between protozoa and fish by eliminating aquatic insect larvae small crustaceae crayfish and fresh water shrimps and once this chain is broken it may take a long time to re-establish a normal fish population. They conclude that a detailed study of the subject should be made.

G Macdonald.

UPHOLT W M GAINES T B SIMMONS S W & ARKOLD E H. The Experimental Use of DDT in the Control of the Yellow Fever Mosquito *Aedes aegypti* (L). Supplement No 186 to Pub Health Rep Wash. 1945 80-86.

The fact that *Aedes aegypti* breeds in water containers which do not contain mud (which inactivates DDT) or fish (which might be killed by large doses) might make it possible to achieve residual larvicidal action against this mosquito. Experiment shows this to be possible and that the efficiency of anti-*Aedes* campaigns can therefore be increased. A great variety of miscellaneous water containers were treated with DDT emulsion concentrates at doses of 1 part DDT per million and over. In all cases residual action was obtained and in some for periods as long as six months. In many cases the containers had been emptied and refilled in the meantime and it seemed that the container itself remained toxic despite the water changes once it had been treated. This conclusion, arrived at in the field, was tested and verified in the laboratory where it was shown that articles sprayed with DDT emulsion and subsequently repeatedly filled and emptied, remained toxic over several months. Similar results were secured when DDT was applied as a 20 per cent. mixture with a wettable powder.

Larvae of *Aedes aegypti* become morbid as a result of exposure to DDT much more quickly than larvae of *Anopheles quadrimaculatus* though they usually survive for a longer period of time. When final mortality is considered there is little difference in the resistance of the two mosquitoes.

The presence of DDT in water or on damp surfaces does not deter mosquitoes from ovipositing. *Aedes aegypti* prefers to oviposit on moist surfaces rather than on water but eggs laid on surfaces treated with DDT hatch normally, most of the larvae however die within three days of hatching. Pupae are not affected by DDT though the vehicle in which it is applied may be lethal to them.

G Macdonald

LINDQUIST, A. W. MADDEN, A. H. HUSMAN, C. N. & TRAVIS, B. V. DDT dispersed from Airplanes for Control of Adult Mosquitoes. *J. Econom. Entom.* 1945 Oct. v. 38 No 5 541-4 2 figs.

This report describes the results of spraying 5 per cent. solutions and emulsions of DDT from a Piper Cub airplane over ground covered with dense mangrove and bush of varying density for the destruction of adult *Aedes taeniorhynchus* which were present in great numbers. The results were assessed by estimating the numbers of mosquitoes attempting to bite test subjects in the areas before and after spraying and in untreated neighbouring areas.

Twelve tests on plots ranging from 8 to 30 acres each with 2 quarts of 5 per cent DDT per acre showed very similar results with emulsions and solutions. After spraying observations were made at 1, 4, 7, 24 and in a couple of cases at 48 hours. At the first observation there was a reduction of about 60 per cent. and this increased at each subsequent count till at 24 hours the reduction varied from 69 to 99.5 per cent. and averaged 88 per cent. This gradual change coupled with the dense vegetation which made direct contact of the falling spray with many mosquitoes unlikely led the authors to believe that lethal action was largely the result of residual films on vegetation and not an immediate effect of the spray.

Dusts containing DDT in similar quantities and scattered from aircraft caused no reduction observable at 24 hours. Two trials with smokes generated by injecting DDT solution into the exhaust pipe gave different results. In one no control was secured, in the other a 98 per cent. reduction was recorded at 24 hours. The authors believe that in this last case there had been poor smoke generation and most of the DDT had been liberated in a spray.

G Macdonald

LINDQUIST, A. & McDUFFIE, W. C. DDT-Oil Sprays applied from an Airplane to control *Anopheles* and *Mansonia* Mosquitoes. *J. Econom. Entom.* 1945 Oct. v. 38 No 5 545-8.

In two tests carried out in the Panama Canal Zone sprays containing 10 per cent. DDT in a mixture of cyclohexanone and oil were distributed from aircraft at doses of 2 quarts per acre over mosquito-infested forest of moderate density. Before and after spraying estimates were made of the numbers of mosquitoes *Mansonia* spp. and *Anopheles* spp. mainly *A. albimanus* attempting to bite test subjects. In each of the two areas there were six observation stations at each of which several counts were made. The averages of the results are shown below—

[August 1946]

First Test			Second Test	
Date	Mosquitoes per man per minute		Date	Mosquitoes per man per minute
	Mosonnia	Anopheles		Mosonnia Anopheles
Before spraying			Before spraying	
13 4	24	1	18 4	4 7
14 4	21	1 3	19 4	4
			After spraying	
After spraying			20 4	0 19
15 4	0 18	0	21 4	0 58
16 4	0 48	0		
18 4	0 64	0 0.5		
19 4	0 63	0 25		
21 4	22	1 12		
23 4				

All larvae in a shallow lagoon, several acres in extent were destroyed in the first test, and no fresh breeding was recorded for a week G Macdonald

KIRK R & LEWIS D J Taxonomy of the Ethiopian Sandflies (*Phlebotomus*)  
I. Classification and Synonymy Ann Trop Med & Parasit. 1946  
Apr. v 40 No. 1 34-51 29 refs

The literature on *Phlebotomus* is scattered, and the insects themselves are difficult to distinguish owing to their small size and to the fact that, recently, workers have used internal characters for the differentiation of species. Knowledge of the African species has tended to advance less rapidly than of those of the Oriental and Mediterranean regions. Kirk and Lewis's series of papers will therefore be very welcome.

The authors classify the Ethiopian sandflies into three sub-genera *Phlebotomus* (restricted), *Synanthus* (*nitroscus* and *Prophlebotomus* Franca & Parrot. The discussion of this classification and of others that have been proposed, takes up the first six pages of the paper. The rest consists of a series of notes on the individual species giving their synonymy, their broad distribution and some comments on the species themselves. No keys or other means for actual identification are provided, and consequently, pending the appearance of keys in further parts of the series the present paper is not to be expected to provide a means for identification though it does provide any worker on the sandflies with a mine of information that may save him from endless burrowing in the literature of the genus.

John Smart

D CRUZ FERREIRA F A reacção das precipitinas aplicadas aos dípteros do género *Phlebotomus* Precipitin Reactions on *Phlebotomus* Species. An. Inst. Med Trop. Lisbon 1945 Dec v 2, 187-96. English summary

YAO Y T & WU C C Notes on the Chinese Species of the Genus *Phlebotomus* Part VI. Sandflies in Chungking, Szechuan, with Description of a New Species, *Phlebotomus holoscutellatus*. J Parasitology 1946, Feb v 32, No. 1 87-90 8 figs. on 1 pl. [12 refs.]

PALMER, E. D. Intestinal Cantharidiasis due to *Tenebrio molitor*. J Parasitology 1946 Feb. v 32 No 1 54-5.  
An infant whose food from the age of three weeks contained cereals began at the age of 4 months to vomit frequently between meals and when 5 months

old began to pass by the rectum larvae identified as *Tenebrio molitor* (the meal worm) the adult beetles were later found in the infant's precooked cereal food. Several of these larvae were passed during 3 months six were recovered and two of them lived for at least two weeks in a dry air tight jar. The child continued to gain weight but fed poorly vomited frequently and had long spells of crying. There was no diarrhoea or melaena and no larvae were vomited. Purges and enemas had no apparent effect and larvae were still being passed 3 months after the first [see also this *Bulletin* 1921 v 17 125 1933 v 30 317] J F Corson

MICHENER C D A Method of rearing Chigger Mites (*Acarina Trombiculinae*)  
*Amer J Trop Med* 1946 Mar v 26 No 2 251-6 4 figs

As yet no really satisfactory method of rearing Trombiculid mites in the laboratory has been devised. It would be valuable to have some such technique for studies of the rickettsiae of scrub typhus carried by Trombiculid mites. This paper describes various techniques which may be useful to workers on this subject but which have produced no notable advances in handling the mites. To obtain fully fed larvae an infested chicken or pigeon is placed in a cage above a dish of water and the parasites which drop off after engorging are easily recovered from the surface of the liquid. They are removed from the surface on small pieces of newspaper by this means they can easily be handled without damage. These larvae are then kept in a glass jar with a thin layer of plaster of paris covering its walls. This gives a suitable humidity without the production of moulds and enables a high proportion of nymphs to be obtained.

The nymphs are kept in a similar jar in a mixture of five parts of sterilized soil with one part of chicken manure. This medium is exposed to the air so that the top surface becomes dry and the mites are discouraged from migrating from it. In about three weeks (at approximately 80 F) some adults were produced, but a fairly high mortality was found and few laboratory produced adults ever laid eggs.

Adult mites caught in the soil in nature readily laid eggs under similar conditions and if the soil-manure mixture was kept firmly pressed the eggs were restricted to the surface layer and were easily found. They hatched to give larvae which could be fed on chickens. Small pieces of wet paper were used to transfer the larvae to the host and when these dried the mites walked on to the skin and attached themselves.

Although some success has been achieved here in breeding the mites it is clear that many improvements of technique will be required before sufficient of these Trombiculid mites can be obtained for laboratory experiments.

Kenneth Mellanby

WILLIAMS R W A Contribution to our Knowledge of the Bionomics of the Common North American Chigger *Entrombicula alfreddugesi* (Oudemans) with a Description of a Rapid Collecting Method. *Amer J Trop Med* 1946 Mar v 26 No 2 243-50 3 figs [11 refs.]

The mite *Entrombicula alfreddugesi* is a common cause of scrub itch in the southern part of the United States. The method described here for collecting large numbers of mites allows as many as 500 larvae to be obtained in one hour. About six white saucers are placed on the ground in likely areas and the reddish coloured larvae are easily visible on the surface. They can be collected without damage by a simple aspirator similar to that used for catching mosquitoes fleas etc.



## BOOK REVIEW

ADRIENS L. [Docteur en Sciences chimiques etc.]. Contribution à l'étude de la toxicité du manioc au Congo Belge. [Study of the Toxicity of Manioc in the Belgian Congo] Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales. Mémoires (Collection in -8°) 1946 v 13 No 4 140 pp. 2 diagrams.

This is an account of work carried out by the Chief of the Laboratory for Chemical Research in the Belgian Congo—it obtained Honourable Mention at the Annual Congress of the Belgian Royal Colonial Institute in 1940. The long delay in publication is no doubt due to the war.

Manioc *Morinda atisissima*. Bitter Cassava is used for its flour for preparing tapioca its starch, cassava cakes etc and it contains a cyanogenetic principle in common with *Phaseolus lunatus* and *Linson unilobatus* whereby on addition of water for example hydrocyanic acid is set free and may cause fatal poisoning.

The author has undertaken an intensive study to determine the nature of the poison the factors which participate in the elaboration of the cyanogenetic heterosides and how these may be destroyed or got rid of. He describes in detail the various ways in which the preparations of manioc are obtained, by maceration, by boiling or by roasting—how by repeated washing by removal of the outer layers or otherwise the poisonous tuber can be made innocuous. These facts are already common knowledge and the author after these preliminaries goes on to describe his personal researches which have been directed to determining, first the action of the emulsion of manioc on the amygdaloidase, Congo manioc containing an emulsin which breaks down the amygdaloidase liberating the hydrocyanic acid. Secondly the action of this emulsin on dimethylcyanhydrin, the synthetic aglycone of the heteroside of manioc thirdly the action of emulsin on the synthesis of aldehydes ketones and glucides with HCN using for this purpose benzoin aldehyde acetone glucose and certain glucidic products. Lastly the action of decomposition products of aglycone on certain glucides. All these are considered and recorded with a wealth of detail described in the letterpress and illustrated with a number of protocols.

The point of chief practical importance is a commercial one. Cassava or manioc is an excellent food but unfortunately in its native state it is toxic. To remove the poison at all events to reduce it to the smallest possible amount careful preparation is necessary and if in spite of all care small quantities of the poison still remain the addition of "proportionally insignificant amounts of glucose will dispose of the danger. The method consists essentially in dividing the tuber (sometimes decorticated, but not always) into cubes or small pieces (*cosettes*) exposing them to the sun the whole day and at dusk placing them where they are protected from the moisture of the night air next day the pieces are dried in a hot-air stove at a temperature of 35–40°C. not higher than the latter otherwise the product becomes brown and scorched-looking. If they are to be consumed at once they should be cut small and left in a large quantity of water to soak this water must be thrown away. For sale the agents need the *cosettes* to be dry really free from all moisture to this end the drying should be rapid and the product protected from dew or the moisture of the night air otherwise the drying process must be repeated moreover moisture will favour growth of mould and bacteria in transit.

This work will have much interest for the agricultural research chemist and, possibly for the toxicologist but makes no practical appeal to medical men.

H Harold Scott

# TROPICAL DISEASES BULLETIN

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## BLACKWATER FEVER—MODERN THEORIES

### A CRITICAL REVIEW

By B G MAEGRAITH B.Sc. D.Phil. M.B. B.S.

*Alfred Jones Professor of Tropical Medicine Liverpool School  
of Tropical Medicine (University of Liverpool)*

#### *Aetiology*

Blackwater fever is still considered on fairly good grounds to be a complication or sequela of malaria. It is most often found in endemic and hyperendemic malignant tertian regions but may be associated with benign tertian or quartan malaria. Plasmodia are found in the peripheral blood in about half the active cases. Blackwater may appear in individuals who have left the tropics and are residing in temperate or cold climates. It may develop subsequently to artificially induced malaria. KITCHEN and SADLER (1945) have recently described such a case in which three plasmodial species were used therapeutically in succession *P. falciparum* being introduced by mosquito bite. In spite of treatment *P. falciparum* persisted in the peripheral blood for about five months. At the end of this period the patient was given a further course of quinine therapy and developed blackwater fever some hours after the first day's treatment. All the malarial strains used in this case were well known and none had any previous history of being associated with haemoglobinuria. The authors therefore suggest that the prolonged parasitaemia may have been an aetiological factor. The quinine administration may also have been significant. The relationship of quinine administration to the onset of blackwater fever has frequently been noted. For instance in the West African Command in 1941-43 haemoglobinuria developed in a high proportion of cases during oral quinine therapy for malignant tertian malaria. Moreover FINDLAY is quoted (SKIPPER and HAINE 1945) as stating that in the same Command the incidence of blackwater fever diminished considerably after the introduction of mepacrine in place of quinine for treatment and suppression of malaria.

Various attempts have been made from time to time to determine the rôle of antimalarial drugs in the genesis of blackwater fever but apart from clinical observations such as those mentioned above the results of experiments on these lines have been equivocal. Recently ZYLMANN (1944) compared the lytic action on human red cells (both from normal and malarial subjects) of equivalent solutions of quinine and atabrin and observed that whereas quinine had a lytic effect on all cells atabrin acted more vigorously on cells from malarial patients. He concluded that atabrin had a true lytic effect. Most authors

however are agreed that atebuin has in fact, very little effective haemolytic action either when given in massive doses or in small doses over long periods (MAGRAITH and HAVARD 1945 Army Malaria Research Unit 1945 etc.)

### Haemolysis

The most striking phenomenon in blackwater fever is the intense haemolysis which involves both parasitized and unparasitized cells. Such haemolysis is closely related to that seen in relatively minor degrees in malaria uncomplicated by haemoglobinuria. The mechanism of its production is not understood. No identifiable circulating haemolysin has so far been isolated, although the early experiments of FOY and KORDI led them at first to conclude that a "circulating haemolysin" existed in the circulation of the blackwater fever patient. These workers (1941) transfused normal red cells into an actively haemolyzing case of blackwater fever and found that the introduced cells were destroyed very rapidly and were therefore apparently as susceptible to lysis as the cells in the patient. An extension of these experiments by FOY and his colleagues (1945) showed that cells from a blackwater fever patient were equally readily destroyed in a normal circulation and further that the plasma from an actively haemolyzing case of blackwater fever did not precipitate a haemolytic crisis when injected into a patient suffering from malignant tertian malaria. These authors have therefore concluded that in blackwater fever the fundamental factor is probably

extracellular and can haemolyse normal cells as well as bring about changes in the blackwater fever cells that render them susceptible to destruction, even in normal circulations. This latter point is emphasized by the further observation of FOY and KORDI (1943) that blackwater fever cells are more fragile than normal cells in a lysolecithin system although as other authors have also reported, their fragility in saline is normal. This increased susceptibility of blackwater fever cells *in vitro* to lysolecithin indicates that this substance may play a part in the haemolysis of blackwater fever possibly by its action on the lipid-protein complex of the cell membrane. There is some evidence *e.g.* the appearance of spherocytes (FOY and KORDI 1943 and others) that this latter may be altered in blackwater fever with concomitant changes in permeability.

A splenic factor has often been considered as a possible agent in the lysis occurring in blackwater fever mainly on the analogy of the part played by this organ in other haemolytic states. VINT (1941) for instance has pointed out that enlargement of the spleen might increase the degree of separation of erythrocytes and plasma in that organ (KIKISLY 1934 FAHRSTUS 1909). Such increased separation would work with existing anaemia (such as for instance that occurring in malignant tertian malaria) towards reducing the effective erythrocyte-plasma interface so that the so-called stabilizing substance (FAHRSTUS) which is thought by some to be lysolecithin\* would be ineffectively adsorbed and thus become potentially active as a lytic or pre-lytic agent. This possibility has been recently discussed by FOY and KORDI (1943) and in more detail by GEAR (1946). The latter author further suggests that the spleen may function in blackwater fever as a reservoir of a hypothetical autohaemolysin (see later). This haemolysin would accumulate when the splenic circulation was impeded, as it is in the enlarged spleen of malaria and might be thrown out suddenly into the general circulation by splenic contraction thus accounting for the sudden onset of haemolysis often seen in blackwater fever.

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\* LASKER and FRIEDMAN (1945) have recently isolated a haemolytic substance from human plasma which is nitrogen- and phosphorus-free and cannot therefore be lysolecithin. *In vitro* haemolysis brought about by this agent is inhibited in a remarkable way by antimalarial drugs, and Lasker suggests that malaria parasites at some stage of their development produce a metabolite closely related to this natural haemolytic substance.

SMITH and EVANS (1943) consider that changes in blood pH may affect the rate of haemolysis. These authors found red cells resistant to saline haemolysis in alkaline solutions and highly susceptible in acid solutions. They suggest therefore that the degree of acidosis occasionally met with in blackwater fever may account for the increased haemolysis. Similar effects of pH have been noted by DACTE and RICHARDSON in cases of chronic haemolytic anaemia with nocturnal haemoglobinuria and recently BIRNBAUM and his associates (1945) have shown that the addition of alkali to bile solution delays its lytic action on both normal and malarial red cells. The latter authors conclude from their experiments that although acidity may thus play some part in haemolysis, sensitivity to lysis is primarily a function of the cell itself and not of its external environment.

An alternative hypothesis has been put forward by MAEGRAITH FINDLAY and MARTIN (1943) who discovered that animal tissue contains a heat labile lytic agent which is normally inhibited by factors present in tissue washings and serum. They suggest that the rate of lysis occurring in an animal at any one time may be a function of the balance between the tissue lytic factor and its inhibitors. Sera from actively haemolysing blackwater fever cases were found by these authors to inhibit the lytic agent much less effectively than normal sera indicating that in blackwater fever the balance between the lytic agent and the inhibitory factors is shifted to the lytic side. In blackwater fever therefore there exists no abnormal lysis rather the lysis is simply a manifestation of excessive uninhibited activity of the normal lytic process. The mechanism of reduction of activity of the inhibitory factors in blackwater fever is unknown possibly the plasmodial infection or the exhibition of antumalarial drugs or both may be concerned. POWDER (1944) has repeated the experiments of Maegraith and his colleagues and has confirmed their findings as far as the lytic effects of tissue are concerned. He considers the tissue lytic agent to be similar to lysocithin. BRICKMANN and WERTHEIMER (1945) have also confirmed the presence of the tissue lytic agent which however they consider is not connected with normal or pathological blood destruction. It is not unlikely that the lytic agent observed by Maegraith and his co-workers is identical with the crystalline haemolytic substance recently isolated from human plasma by LASER and FRIEDMAN. Evidence of a similar lytic factor has also been recorded recently by BROWN *et al* (1944) in the course of an investigation of the fate of transfused red cells in various forms of anaemia.

Recently GEAR (1946) has suggested that the lysis in malaria and blackwater fever may result from a haemolysin developed as the result of the plasmodial invasion of the red cells. On the analogy of the experiments of SCHWENTER and COMPTON (1939) who found that emulsions of homologous kidney and brain were autoantigenic if injected into rabbits after being mixed with bacterial toxins GEAR suggests that the red cell when invaded by plasmodia may become autoantigenic, giving rise to an autoantibody (haemolysin) which in the presence of complement is able to lyse homologous red cells. A somewhat similar suggestion has been made by BUTTS (1945) who believes that a factor concerned in the haemolysis of blackwater fever may be iso-immunization to an Rh like substance present in malarial plasmodia. His assumption is based on what he states to be the comparative incidence of blackwater fever and erythroblastosis foetalis in white and negro races. BENIANS (1944) has also pointed out the possible rôle of autoantibodies in blackwater fever considered purely as a haemolytic disease. He considers that the presence of such antibodies is indicated by the difficulties encountered in cross-grouping the blood of blackwater fever patients for transfusion.

OLIVER-GONZÁLEZ (1944) has suggested that the malaria parasite may contain an antigen related to human isoagglutinogens and that autoagglutination

which is frequently met with in blackwater fever may result from immunization with such a substance. There is some evidence that the malaria parasite can behave in this way, as  $\alpha$  and  $\beta$  agglutinins are often increased during the disease. This author found cold agglutinins in the sera of two cases of blackwater fever. It is interesting to note here that BEXIAVS has demonstrated similar cold agglutinins in severe Raynaud's disease.

A good deal of the pigment liberated by haemolysis in blackwater fever is removed by phagocytosis by reticulo-endothelial cells and converted into bilirubin which is absorbed by the liver cells in the usual way and eventually appears in the bile. Some degree of hyperbilirubinaemia is thus not uncommon in blackwater fever. When the haemolysis is so severe that the normal mechanisms cannot deal with all the liberated blood pigment, the degree of hyperbilirubinaemia is such that the patient becomes jaundiced. Some of the excess haemoglobin pigment is passed in the urine as oxyhaemoglobin (red common in alkaline urine) or methaemoglobin (dark reddish brown common in acid urine) but some remains in the plasma in the form of oxyhaemoglobin and methaemoglobin.

FAIRLEY and BROWFIELD (1934) investigated the pigments present in the plasma of blackwater fever cases and found evidence to suggest that haemolysis was mainly intravascular, the plasma methaemoglobin being apparently derived from the haemoglobin of the lysed cells. These authors observed a further peculiar haemoglobin derivative in one of their cases which they later called pseudo-methaemoglobin. This pigment was found to be present constantly in severe blackwater fever and in a series of elegant experiments FAIRLEY (1938, 1939, 1941) showed that it is formed from free haemoglobin after massive intravascular haemolysis and can be synthesized in man and monkeys after intravenous injection of alkaline haematin. Methaem-albumin as this new compound is now called, does not pass through the kidneys. It is apparently ultimately removed from the plasma by the liver.

### Renal Function

About half the deaths in blackwater fever are associated with kidney failure (STERNES 1937). Renal function may become affected at any stage of the disease independently of the passage of haemoglobin in the urine. Failure is indicated first in most cases by a reduction in urinary flow which may go on to complete anuria. Recovery from anuria is rare and is usually followed by polyuria which may last a week or more. During this period the concentration of the urine is greatly reduced indicating renal tubular damage.

There has been extensive controversy over the mechanism of the production of renal failure in blackwater fever. Some authors consider that methaemoglobin in the presence of acid urine and an adequate concentration of salt gives rise to insoluble acid haematin which deposits in the renal tubules and so mechanically obstructs the flow of urine. MARGRAITH and FINDLAY (1944) and others have however pointed out that anuria frequently develops at a time when no blood pigments are being passed, that the salt content of the urine in blackwater fever is nearly always well below normal and that the urine is often alkaline or neutral when anuria supervenes. Again, heavy albuminuria with acid urine by no means invariably leads to anuria. These and similar observations have led many authors to the conclusion that the anuria of blackwater fever cannot be adequately explained on the grounds of mechanical obstruction by haemoglobin products (GEORGOPOULOS (1933) JOURNE (1944) PETERS (1945) etc.). In the search for a more satisfactory explanation a great deal of attention has been paid to the action of circulating haemoglobin and (because of the similarity between the kidney failure in blackwater fever and that in crush syndrome)

myohaemoglobin on kidney function. For instance YULE GOLD and HINDS (1945) injected solutions of haemoglobin into rabbits which were secreting acid or alkaline urine and in which the kidney tubules were previously damaged either by temporary clamping of the renal pedicle (which was shown by SCARFF and KEELE (1943) to produce renal cortical lesions) or by previous poisoning with sodium tartrate. These authors concluded from their experimental results that precipitation of haemoglobin in the renal tubules is not primarily dependent on the reaction of the urine but on non specific functional abnormality of the individual nephron which could be produced either by the ischaemia or by chemical poisoning. Given the renal tubular damage and haemoglobinuria however pigmented casts were more common in animals secreting acid urine than in those secreting alkaline urine. BYWATERS and STEAD (1944) recently reported that myohaemoglobin from dogs can similarly produce renal damage in shocked rabbits excreting acid urine leading sometimes to anuria and death. These and similar experiments have shown that circulating haemoglobin and related pigments may under certain conditions be associated with renal failure but in otherwise normal animals injection of these pigments has been found to have very little renal effect.

The existence in many diverse clinical conditions of the symptom-complex of oliguria or anuria associated with nitrogen retention and inability to concentrate urine and frequently accompanied by degenerative changes in the renal tubules but not necessarily related to the passage in the urine of blood or muscle pigments has led MAEGRAITH and his colleagues to suggest that the renal failure in blackwater fever may be due to some cause other than the circulating pigment which is common to many other conditions. For reasons outlined below these authors consider that the basis of such kidney failure is renal anoxia.

ALLEN pointed out in 1926 that the histological picture seen in kidney failure in acute malignant tertian malaria was similar to that of the later stages of blackwater fever the outstanding feature being marked degeneration of the cells lining the renal tubules. Such changes were not due to the malaria parasites themselves which are usually scanty in renal tissue even when abundant elsewhere in the body. Many authors from time to time have tried to incriminate toxic substances liberated by the parasite during its development or by the destruction of red cells at sporulation, but attempts to define this malarial toxin which is presumably present also in blackwater fever have all failed. For instance LINTHAREFF (1937) suggested that plasmodia produced a toxin which reversibly combined with haemoglobin to form a compound which acted directly on the renal tubular epithelium giving rise to degenerative changes. He attempted to prove his theory by comparing the effects on the renal function of guinea-pigs of injection of haemoglobin solutions obtained from normal and untreated malarial subjects. His results and others of an equally equivocal kind leave the question of the existence of a soluble malarial toxin still unsolved. In the present stage of our knowledge it is therefore necessary to look elsewhere for the explanation of the kidney lesions in malaria and blackwater fever. RIGDOV (1942) has put forward the view that the lesions of malaria result fundamentally from a state of anoxia in the tissues concerned. Such tissue anoxia may arise from lysis of red cells or interference with their oxygen carrying capacity or may develop as the result of alteration of the capillary blood flow through the tissue arising from stasis or mechanical obstruction (e.g. by autoagglutinated and parasitized cells) or from generalized vascular constriction or collapse such as is seen in shock. According to RIGDOV's hypothesis therefore anoxia of the renal epithelium in blackwater fever may result in part from the malarial anaemia and in part from reduction in the effective tubular blood supply brought about not by physical obstruction by

agglutinated parasitized blood cells (which are rarely seen in large numbers in the kidney) but by changes in the intrarenal blood flow associated with peripheral vascular disturbances of a general nature. SCARFF and KEELE (1943) have shown recently that degenerative changes can be produced in the renal tubular epithelium of the rabbit by restricting the blood flow to the kidney and have noted the similarity between the lesions so produced and those seen in crush syndrome. Many authors have commented on the close resemblance between the lesions seen in the crush syndrome and blackwater fever (BYWATERS and BEALL, 1941; BYWATERS and DIBLE, 1942) so that it is possible that renal ischaemia may also play a part in the production of lesions in blackwater fever. Changes in renal blood flow have not yet however been demonstrated in blackwater fever but there is some clinical evidence that they occur in other conditions in which the syndrome of renal failure may develop such as traumatic shock (LAUSON *et al.* 1944). The investigation of the renal circulation in malaria and blackwater fever by means of clearance tests would add considerably to our knowledge in this respect.

### *Treatment*

*Antimalaria drugs*—Although the disease is generally considered to be a complication of malaria most authorities consider that antimalaria drugs should not be given in blackwater fever. However where parasites are present it may be dangerous to leave the malaria untouched. There thus seems to be no reasonable argument against using antimalaria drugs under such conditions provided the drugs are not themselves possible haemolytic agents. As stated above quinine is suspect and there is similar evidence to show that primaquine may also actively stimulate haemolysis. There is however no evidence of any value indicating that atebem is a haemolytic drug or has any effect on haemolysis *in vivo*. The drug can be taken as a suppressive for very long periods without haematological effects—it can be given in large doses orally or intravenously without haemolysis—it is said to stimulate the haemolytic effect of specific haemolytic antibodies (ZILMAN 1944) but the evidence for this is poor. Finally experience has shown that atebem can be given safely in blackwater fever. If it is employed it should be given in adequate dosage and not limited to small and innocuous but equally ineffective doses as sometimes recommended.

When parasites are not found in the peripheral blood, antimalarial therapy is not indicated. Frequently parasites appear after haemolysis has ceased and the patient has begun to recover. Under these circumstances again atebem is indicated in full dosage.

*Replacement of fluid and salt*—Fluid and salt may be lost by the patient in large quantities as a result of excessive sweating, vomiting or watery diarrhoea. As far as possible fluid loss (urine, liquid faeces, vomit) and fluid intake (including of course parenterally administered fluid) should be estimated and the intake must be roughly balanced against the output. It is a serious mistake to push fluids too vigorously—the patient, especially when anuric can only too easily be waterlogged, with resultant oedema and circulatory complications (PARAMORE 1945 *Bull U.S. Army Med Dept.*, 1945; MACGRAITH, 1945). Fluids should be given when possible by mouth. If vomiting or coma prohibits this intravenous infusion by drip of physiologically balanced saline solution is indicated. The infusion should be given slowly and the amount must be controlled by the output intake balance.

*Transfusion*—As a good working rule it can be reckoned that if the red cell count is 1.5 million per cmm the carriage of oxygen to vital tissues is dangerously reduced. This makes transfusion necessary. Replacement of red cells can be

carried out by transfusion of citrated blood by direct arm to-arm transfusion or by injection of a concentrated cell suspension in physiological saline. The injection of citrated blood is liable to give rise to severe reactions with rigors due to so-called pyrogens. Direct transfusion is difficult in tropical conditions owing to sweat dust etc. Injection of concentrated cells is the best method if facilities are available. The fluid given with the transfusion must be calculated in estimating the daily fluid intake. As pointed out elsewhere the agglutinins of the plasma may be increased in malaria and blackwater fever and autoagglutination is common. It is necessary therefore before transfusion to cross match the donor's corpuscles with the patient's serum and vice versa. Grouping is not in itself sufficient.

SMITH and EVANS (1943) have stated that transfusion is inadvisable when oliguria or anuria is present. This advice is apparently based on the possibility of lysis of the donor's cells. Such lysis does sometimes occur but it is seldom severe and must be risked if the patient's corpuscles are so few that the oxygen carrying power of the blood is seriously reduced.

**Alkalis**—Intensive alkali treatment of blackwater fever based on the mechanical blockage hypothesis of BAKER and DODDS (1925) was first employed by HANSCHALL in 1925. The object of such therapy is to produce an alkaline urine and so to minimize the precipitation and deposition in the renal tubules of haemoglobin and its derivatives so that mechanical blockage of the uriniferous tubules is prevented and anuria thereby avoided. Such therapy has been enthusiastically recommended and has had many advocates in recent years some of whom go so far as to advise enough alkali to produce Trousseau's sign (SMITH and EVANS 1943). MAEGRAITH and his colleagues have recently criticized the basic hypothesis upon which alkaline therapy is founded and have pointed out that since the introduction of this form of treatment the death rate from blackwater fever has risen not fallen. These authors point out that the frequently repeated advice that alkali should be given until the urine becomes alkaline is unsound since where kidney function is damaged the reaction of the urine may remain unaffected by large doses of alkali. In any case it is not established that anuria is less likely to develop if the urine is made alkaline (MAEGRAITH and HAVARD 1944). Alkalis are usually administered as sodium salts commonly the bicarbonate or citrate or both. In reasonable doses e.g. not more than 20-30 gm. in 24 hours these salts are not contra-indicated and may be useful in promoting mild diuresis. Given in large doses they may be dangerous (ARMY MALARIA RESEARCH UNIT 1945). Alkalis are best given by mouth, but may be administered intravenously as sodium bicarbonate solution (150 grains to the pint). Sodium lactate may also be given intravenously.

The use of alkalis has also been advocated for dealing with the acidosis which is frequently said to be present in blackwater fever. The available evidence does not altogether support this contention. Acidosis although occasionally reported (FAIRLEY and BROMFIELD 1933. FOY KOVDI and MOUMJIDIS 1941) is not commonly seen in either malaria or blackwater fever.

**Other substances**—The successful treatment of blackwater fever with anti-venene has again been reported recently by SINGH and SINGH (1943) but the evidence brought forward is unconvincing. BURKITT (1943) has used sodium luminal [Phenobarbitonum Solubile] grams 8 to 10 intramuscularly with good results and quotes a series of 30 cases of blackwater treated successfully by GREGORY with intravenous injection of 15 grains of that drug. GEAR (1946) believes that the apparent success of such treatment results from the sedative action of these drugs which minimizes splenic contraction and may thus prevent flooding of the circulation with (hypothetical) autolysin.



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## SUMMARY OF RECENT ABSTRACTS \*

### VII HELMINTHIASIS.

[Continued from p 701]

#### Nematodes

*Hookworm Infestation etc*—FERRO-LUZZI (p 478) claims that until recently the problem of ankylostomiasis has not arisen in Eritrea but that owing to the movements of troops and labourers from other countries parts of Eritrea are now becoming endemic foci.

SMIRKOV (p. 135) has made studies on the rate at which hookworm larvae penetrate the skin of the hamster.

FLEMING (p. 48) reports a case of intractable diarrhoea with high eosinophilia due to hookworm infestation apparently contracted after a single exposure to infective mud.

From the study of the records of a large number of cases of hookworm infestation KAMMER (p 48) concludes that fever is a very uncommon symptom. Eosinophilia was a pronounced feature in a large proportion of patients admitted to a U.S. base hospital in the South Pacific during 1942-43. As a result of studies made on these cases ALLEN (p 49) concludes that hookworm infestation was largely responsible for this eosinophilia. CRUZ and DE MELLO (p 1020) report but cannot explain a diminution of the excretion of sodium chloride in the urine of patients with hookworm anaemia.

In *Army Medical Department Bulletin No 47* (p 742) it is noted that the recommended treatment for hookworm infestation [for adult British males, presumably] consists of 4 cc. tetrachlorethylene and 1 cc. oil of chenopodium this draught being taken on an empty stomach and being followed if necessary by a dose of Epsom salts a few hours later.

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945 v 42. Refer once to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

DUVOIR and BRUMPT (p. 913) describe the artificial infestation of patients suffering from polycythaemia with larvae of *Ancylostoma duodenale*. The effect of this infestation on the disease was apparently beneficial, the number of red cells being reduced and the symptoms relieved, in a few days.

EDKHORN *et al.* (p. 911) have made five surveys of children in the Gorgas Hospital Panama Canal Zone—they were infested with one or more of the common intestinal nematodes. MILLER *et al.* (p. 912) refer to these cases noting that there were some infections with *Strongyloides stercoralis*.

WHITEHILL and MILLER (p. 576) describe a patient in whose urine larvae of *Strongyloides stercoralis* were found on several occasions though they were absent from the faeces. The origin of the infection was not discovered. Treatment with gentian violet was successful. EXGEL (p. 49) describes a case of infestation with *Strongyloides stercoralis* in which apparent cure was obtained by means of gentian violet (1 per cent. solution) introduced slowly (50–60 drops per minute) into the duodenum. A dose of 250 cc gave rise to continuous retching and slight collapse but subsequent daily doses of 100 or 50 cc, given more slowly for 5 days, apparently completed the cure. PALMER (p. 133) describes a case of infestation by *S. stercoralis* in which apparent cure was obtained by means of gentian violet given in enteric-coated tablets. The patient died (apparently of tuberculosis) but no *Strongyloides* could be found post mortem—larvae had been found in the faeces before treatment was started.

HASIMOV (p. 50) describes for the first time infestation of man by *Ostertagia ostertagi*, normally a parasite of cattle and sheep. He describes the specimen found. In comment LAPAGE suggests that the worm may have been merely a passenger in the human intestine.

TSUCHIYA and RÜLLER (p. 817) report a case of infestation with *Trichostrongylus* in the United States where it is exceedingly rare though not uncommon in the sheep- and goat-raising areas of India and in Japan. They discuss the identification of the eggs of *Trichostrongylus*.

*Ascariasis etc.*—GUTH (p. 51) writing in a Swiss journal remarks that human ascariasis has increased enormously since the end of the war of 1914–18 and he suggests that this may be due to increased consumption of uncooked foods which are often grown in gardens fertilized with human excreta. He describes two fatal cases in which these worms were found in the bile ducts within the liver. Treatment with anthelmintics is not capable of destroying the worms in the bile ducts and surgical removal of the worms with drainage of the bile ducts may be necessary.

CHANG and CHIN (p. 744) observe that in Szechwan China vegetables are grown in soil fertilized with human faeces and are frequently contaminated by the eggs of *Ascaris*. They have shown that the process of pickling in brine which is a common procedure for the preservation of these vegetables does not ensure that all the eggs are destroyed. The infection may therefore be spread by the consumption of pickled vegetables though other sources of infestation are no doubt, more important.

EDKHORN *et al.* (p. 914) discuss a series of children infested with *Ascaris* and seen at the Gorgas Hospital Panama Canal Zone—most of them were in hospital because of other diseases of which the commonest was malaria. As usual, there was a high incidence of *Ascaris* infestation in early life. The symptoms are discussed [but the association with other diseases obscures them] the authors commenting that anaemia is not one of them and that eosinophilia is no index of the severity of infestation. The drug of choice for treatment is hexylresorcinol. Details are given of cases in which *Ascaris* was regarded as the cause of death.

The complications due to *Ascaris* infestation as observed at autopsy are discussed by UNGAR (p 745) He reports eight cases in three of which there was intestinal obstruction with gangrene in one invasion of the common bile duct in one invasion of the pancreatic duct and in three toxic damage to the intestinal wall probably due to substances produced by the disintegration of dead worms In most of these the serious complications probably depended not so much on the numbers of worms as on the coincidence of other pathological factors Details of these should be sought in the original

GRAM and HICKS (p 818) have demonstrated that eggs of *Ascaris lumbricoides* are very resistant to sludge digestion either aerobic or anaerobic even after 6 months about 10 per cent of the eggs are still viable Drying in sludge kills them and they cannot survive a reduction of moisture to below 5 per cent Heating the sludge to 50°C for 20 minutes kills half the viable eggs and to 103°C kills them all

VINNITZKY (p 746) has introduced living or dead *Ascaris lumbricoides* and *Toxocara canis* into the peritoneal cavity of certain animals to study the reactions obtained The findings cannot satisfactorily be summarized, and those interested should consult the original abstract

MUKERJI and BHADURI (p 919) describe a case of gnathostome infection of the eye in Bengal The infection was associated with orbital cellulitis and iritis which cleared up when the worm was removed The authors think that this belonged to the new species previously described by MAPLESTONE In man both adult and larval forms may be found the natural hosts are the cat and the dog and man is probably infested by eating infested *Cyclops* or fish

*Filariasis*—CAUSEY *et al* (p 647) examined 5 000 persons at Belem Brazil where filariasis has long been prevalent an infection rate of some 12 per cent was found but the elephantiasis rate was only a fraction of this The chief vector is *Culex fatigans* which is also the commonest mosquito but *Anopheles darlingi* and *A. aquasalis* were also found infected in nature *C fatigans* breeds well in polluted water and one measure of control therefore would be the improvement of general sanitation and drainage

In American soldiers in the South Pacific ENGLEHORN and WELLMAN (p 819) calculate that the shortest period between infection with *B. bancrofti* and the appearance of symptoms was 3 months and that severe symptoms take 8 months to appear The earliest symptoms are general the local symptoms occurring later All the patients in this group had funiculitis many had orchitis and epididymitis a few had lymphadenitis and lymphangitis

KING (p 304) writes from an experience of 268 cases of early filariasis in American soldiers The incubation period appears to vary from 3 to 16 months The first symptoms are pain, swelling or redness of an arm or leg or pain and swelling in the scrotal region Sometimes there is slight fever and the later symptoms may be classified as lymphangitis of the trunk or extremities acute inflammation of the scrotum or its contents and enlargement of lymph nodes No microfilariae were found in the blood of these patients The author thinks that clinical diagnosis is reliable, but has had fairly satisfactory results from the use of an intradermal test

FOGEL and HUNTINGTON (p 53) describe the genital manifestations of early filariasis as they have seen them in members of the American forces in the South Pacific no microfilariae were found in the blood or tissue fluids Some constitutional symptoms were observed and the signs included swelling and oedema of the spermatic cord inflammation of the testes and adnexa hydrocele oedema of the scrotal skin and inguinal adenitis No satisfactory drug treatment was discovered but rest and support were beneficial Operations on hydrocele, hernia and varicocele are contra indicated

GLAUSER (p. 479) also discusses filariasis in American Marines who served in Samoa. He observes that the psychological aspect of the disease was of considerable importance but implies that the fears engendered were largely illusory—there is no evidence that impotence or sterility is caused, and it is improbable that elephantiasis will develop in these men. No form of treatment was found to be effective.

JOHNSON (p. 478) reports on filariasis in U.S. marines from the South Pacific. He makes the point that the longer the time these men spend in the United States after infection the greater the improvement in their condition.

HODGE *et al.* (p. 1020) found microfilariae in two of 268 American soldiers with filariasis. They estimate that in a detachment of soldiers exposed to infection for about one year though only 11 per cent were found to have typical signs, the rate of infection will eventually prove to be in the neighbourhood of 50 per cent. Descriptions of the clinical signs and of a skin test are given.

ZUCKERMAN and HIBBARD (p. 480) have examined lymph nodes removed from patients with early filariasis. They state that biopsy is not necessary for diagnosis in most cases but may be useful in some. Sections showed marked hyperplasia of the reticulo-endothelial cells with hyperplastic and obliterative endolymphangitis even in lymphatics in which acute lymphangitis had not clinically been present. This suggests a general reaction to a toxic product of the worm itself. Eosinophilia was intense in glands in which the filariae were also present, but not in others. There was no evidence that lymphangitis was due to bacterial infection. WARTMAN (p. 305) describes the pathological appearances of the lesions in lymph nodes and in lymphangitis from some of the patients mentioned by Hing above. There is granulomatous inflammation around the worms and in the lymphatic sinuses.

CLEARKE (p. 915) describes the technique and results of a skin test for filariasis in which he uses an antigen prepared from *Dirofilaria immitis*. This test gave positive results in 91 per cent of a group of infected persons but has the disadvantage that it is not specific for *W. bancrofti*—it may be positive in subjects with *Loa loa* or *O. rotundus* or even with *Trichuris* or *Trichinella*. Nevertheless, a positive test in conjunction with clinical symptoms of filariasis in an area in which *W. bancrofti* is known to occur can be taken as confirmation of the diagnosis of filariasis. OLIVER-GONZÁLEZ and BERCOVITZ (p. 219) have tried a precipitin reaction in filariasis, with an antigen prepared from microfilariae of *W. bancrofti*. The results were poor.

BYRD *et al.* (p. 479) give an account of the mosquitoes of the Samoan islands, and of their relation to *W. bancrofti*. Larvae of the latter were found in *Aedes scutellaris pseudoscutellaris* [*Aedes variegatus*] and *Culex fatigans* but these larvae were in the infective stage only in the former mosquito in nature. VEXNER (p. 478) found *Aedes aegypti*, *Aedes scutellaris pseudoscutellaris* [*Aedes variegatus*] and *Culex annulirostris* on two islands of the Ellice group in which filariasis is endemic.

SCOTT *et al.* (p. 917) though recognizing that microfilariae have practically never been found in the blood of American soldiers who served in the South Pacific [but see HODGE *et al.* above] have tested the infectibility of certain mosquitoes indigenous to California. They conclude that *Culex fatigans*, *C. erythrorhax* and *C. tarsalis* would be vectors if opportunity occurred.

BROWN (p. 53) treated 12 patients infected with *W. bancrofti* with anthiomaline, 10–50 cc. (60 mgm. per cc.) being given over a period of 13–26 days. Of the 11 in whom microfilariae were found there was great reduction in the microfilarial count in 10 four to five months after completion of treatment. Anthiomaline is not the ideal drug for this disease but these results indicate that further investigations of its value should be made.

JAFFE (p 918) notes that X-ray therapy in cases of filariasis does not appear to influence the course of the disease though some small benefit is given

YU and MAO (p 747) record *H. malayi* infection in a man who was reported never to have lived outside the provinces of Hupeh and Szechwan in China. *Culex fuscans* is susceptible to infection with microfilariae of *H. malayi* but HU (p 918) thinks that it would not be important in the lower Yangtze region because it seldom enters houses or feeds on man.

FRANKS and STOLL (p 916) describe a technique for the isolation of microfilariae of *D. immitis* and the preparation of an antigen from them for use in a precipitin test. Parallel tests with an antigen prepared from adult *D. immitis* gave comparable results but the authors think that the larval extract actually obtained was not so strong as the larvae were capable of furnishing.

SCHNELLE and YOUNG (p 52) have investigated the periodicity of microfilariae of *Dirofilaria immitis* in dogs. The microfilariae appear in the blood about 8 months after infection and there are two daily peaks, the maximum being in the evening. This pattern can be changed by altering the time of the principal meal of the day. Exercise has no apparent effect. The authors quote evidence which suggests that the spleen is a reservoir for microfilariae.

BRADY *et al* (p 747) have traced the fate of injected antimony in dogs infected with *D. immitis* by using compounds prepared from radio-active antimony. Nearly all the antimony left the blood in a few hours and the greatest concentrations were found in the liver and thyroid. Antimony was also found in the adult worms. After 36 hours the amount excreted in the urine might reach 20 per cent of the total injected.

CULBERTSON and ROSE (p 136) have found Neostam and Neostibosan to be effective against the filarial worm *Leishmanoides carinii* of the cotton rat.

NETTEL (p 54) notes that microfilariae of *Onchocerca* may be found in skin or subcutaneous tissues far from the site of a nodule and that on the other hand even in the presence of nodules the skin may be negative if the worms are immature or unfertilized. GERMAN (p 819) describes a silver stain which gives better definition of larvae of *Onchocerca volvulus* than those commonly used. He describes the morphology of the larvae as displayed by this stain.

RODHAIN (p 820) describes the pathological appearances of the lymph glands and skin in cases of onchocerciasis.

GARRATT (p 649) describes two patients in Nigeria each complaining of upper abdominal pain, and in each of whom liver puncture revealed the presence of large numbers of larvae of *Acanthocheilomonema perstans* though these were not found or were scanty in the peripheral blood. He therefore thinks that this infection was the cause of the symptoms. The second patient was treated with anthiomaline and the numbers of larvae in the liver diminished greatly.

RODHAIN (p. 821) has found *Agamofilaria streptocerca* in Africans of the Belgian Congo.

*Enterobius infestation*—LANE (p 400) discusses infestation with *Enterobius* showing that much is still to be learned about its life-history and that treatment and prevention of infestation are still far from satisfactory.

MILLER and EINHORN (p 578) discuss *Enterobius* infection in children seen at the Gorgas Hospital in the Panama Canal Zone. There is apparently a relatively high incidence in white children as compared with negroes and those of mixed races in spite of the better living conditions of the whites. This has been observed before in the United States. Treatment by tetrachlor ethylene was useless. Quassia enemata were valuable but gentian violet was the best drug.

SCHÜFFNER and SWELLENGREBEL (p. 923) have devised a method of examination which in their hands has given better results than the NIH swab and

other techniques. They use a glass pestle ground slightly rough with which they massage the perianal skin moistened with water. The emulsion thus formed is transferred to a slide and either examined under a coverslip or dried and subsequently examined in cedar wood oil. This method is much quicker than the NIH technique and the authors claim that a simple washing procedure removes all *Enterobius* eggs from the pestle. By the pestle examination more positive results are usually found than by other techniques and more eggs are seen. The same authors (p. 924) discuss further the detection of eggs of *Enterobius* in various situations. They produce more evidence that the pestle method is better than the NIH swab method, pointing out that the preparation of the faecal emulsion which results from the use of the pestle breaks up the clusters of eggs and facilitates detection. Examination of dirt from beneath the finger nails shows eggs quite often but cannot replace the anal examination—the fact that eggs are found there has an epidemiological importance. Samples of dust from schools in Amsterdam have shown very large numbers of eggs especially in water-closets and in dining rooms but it is doubtful if eggs found in dust can develop if swallowed. For the examination of dust the authors prefer a flotation method with zinc chloride solution of specific gravity 1.33. Many details of technique are given in this paper.

PETERSEN and FAHEY (p. 920) have made an extensive survey of *Enterobius* infection in patients in a State mental hospital in the United States. Examinations repeated many times in subjects who gave negative results were made by applying microscope slides to the anal mucosa and the muco-cutaneous junction as this technique was found to be as accurate as and much more rapid than, the standard methods. In all, 59 per cent. of the inmates were infested, but the rate was much higher in those with chronic mental illness. Treatment with gentian violet repeated if necessary, was very successful. Details of the doses used are given in the original abstract.

In a study of the effect of different temperatures and degrees of humidity on the eggs of *Enterobius vermicularis* HELLER (p. 579) has shown that the optimum conditions for development are a temperature of 34–36°C. and a humidity of 90–100 per cent. Higher and lower temperatures and dry conditions reduce the proportion of eggs able to hatch out infective larvae. Ventilation and drying of rooms therefore reduce the chances of spread of this infection. The conditions on the perianal skin appear to be close to the optimal for development.

LATENDJA and CARPANELLI (p. 137) discuss the question of appendicitis and infestation with *Enterobius* without arriving at any firm conclusions.

TRICHINIASIS.—PIGOUY (p. 400) reports an outbreak of trichiniasis in Beyrouth which is practically the only part of Lebanon in which pigs are reared. MÖRNING (p. 401) quotes evidence which shows that trichiniasis is very rare in the pigs of South Africa.

MAZZOTTI (p. 219) has found that compression of 10 gm. of muscle gives better results in the detection of *Trichinella* infection than compression of a smaller quantity and digestion of a larger. As a result of his investigations he estimates the incidence of this infection in Mexico City at about 12 per cent.

MAZZOTTI and LOZANO HURE (p. 55) have carried out a series of tests for trichiniasis in Mexico by means of the intradermal reaction of Bachman. They give details of their results but point out that these vary according to the standards laid down by different authors for a positive result. It is evident that more precise data are required before this test can correctly be evaluated.

GAASE (p. 481) reports a case of infection with *Trichinella* in which the complement fixation test was positive 15 days after the first appearance of symptoms—the test was also positive with cerebrospinal fluid of the patient,

who had shown signs of meningeal irritation and cerebral involvement due probably to toxins since no larvae could be detected in the brain substance.

TALICE (p 305) discusses the symptoms of trichuriasis there is no typical picture but oedema of the face or of other parts muscular pains diaphragmatic signs loss of weight digestive hepatic or gastric signs and eosinophilia are relatively common.

WENDEROTH (p 482) writes of the lesions of the cardio-vascular system in trichuriasis noting particularly the occurrence of thrombosis in the lung mesenteric veins sigmoid sinus and saphenous vein Myocarditis is common but no larvae were seen in the heart muscle in the series of cases in the German army under consideration.

MATOFF (p 579) has investigated the effects of introducing larvae of *Trichinella* into dogs by various routes in relation to any possible age immunity. The original abstract should be consulted.

LISBOA (p 817) reports infestation with *Diectophyme renale* [*Eustrongylus gigas*] the largest of the parasitic nematodes in a woman who passed a male worm in the urine. Infestation with this worm is very rare and its life history is not known.

HAWKINS and COLE (p 912) describe work on the precipitates which form round the body orifices of exsheathed larvae of certain parasitic nematodes when they are immersed in the serum of previously infected animals.

Charles Wilcocks

## MALARIA

DOELEMAN H. De malaria-epidemie te Middelburg in de jaren 1940 tot en met 1945 benevens een onderzoek van parasietendragers. This book is reviewed on p 875.

Soto H. Reconocimiento paludico en una region del Valle de Medellin Antioquia Colombia SA [Malaria Survey in the Medellin Valley Antioquia, Colombia.] 25 pp 6 graphs 5 maps & 9 pls [51 refs] 1945 Oct Bogotá Talleres Graficos Mundo al Dia.

This is a malaria survey report of Medellin and Itagüí two towns whose suburban extensions have met making them a single agglomeration of 173 300 inhabitants. It lies high up in the middle of the valley of the Medellin River Colombia the inhabited area ranging from 1 455 to 1 950 metres above sea level. It has a very equable climate the annual mean temperature is 22.4°C with very slight seasonal variation.

An examination of 3 700 individuals from 5 to 19 years of age revealed a spleen rate of 22.1 per cent. Malaria parasites were found in the blood of 309 individuals 8.3 per cent. *P. vivax* 289 *P. falciparum* 35 (15 mixed infections). *P. malariae* was not seen. Four species of *Anopheles* were found. *A. eiseni*, *A. pseudopunctipennis*, *A. punctimacula* and *A. argyritarsis*. *A. eiseni* was found breeding in only a limited area which is not malarious. *A. pseudopunctipennis* and *A. argyritarsis* were found breeding in abundance. *A. pseudopunctipennis* formed more than half of the total anopheline larvae identified. Neither of these two species appears to have any predilection for human blood and neither was found frequenting human dwellings in any numbers. They are unimportant as vectors of malaria in Medellin. *A. punctimacula* on the other hand predominated in captures in human dwellings. Of 684 females so captured oöcysts were found in 12.18 per cent. It is the chief malaria vector in Medellin and Itagüí.

Norman White



REY H. SOTO, H & HUFFAKER, C. B. *Anopheles punctumaculata* D & K. as the Vector of Malaria in Medellín, Colombia, South America. *Amer J Trop Med.* 1945 Nov., v 23 No 6 501-5 [24 refs]

ALBERTO ALVARADO C. Memoria de la dirección general de paludismo correspondiente al año 1944 [Report on Malaria in Tucumán for 1944.] 72 pp 1945 Tucumán, República Argentina. Ministerio del Interior Dirección Nacional de Salud Pública.

BLACK, R. H. A Preliminary Note on the Cultivation in Vitro of New Guinea Strains of Human Malarial Parasites. *Med J Australia* 1945 Dec. 29 v 2, No. 26 500-501

Blood serum is obtained by placing 20-30 cc. of blood in a large test tube containing 0.1 cc. of 50 per cent glucose solution, and stirring for 5 minutes till defibrination is complete. The serum is separated by centrifugation and placed in a flat bottomed tube about  $\frac{1}{4}$  inch in diameter to give a column of serum  $1\frac{1}{4}$  to 2 inches high. Red cells infected with *P. falciparum* are obtained from beneath the leucocyte layer after centrifugation. These are introduced into the bottom of the serum tube, which is incubated at 37°C. During the course of 28 hours schizogony followed by invasion of new red cells, was observed. At 78 hours forms which resembled gametocytes appeared. At five days parasites were scanty but subculture into fresh serum containing red cells and glucose gave a result similar to the initial culture. C M Wexon

HEIDELBERGER, M., MAYER, M. M & DEMAREST C. R. Studies in Human Malaria. I. The Preparation of Vaccines and Suspensions containing Plasmodia. *J Immunology* 1946 Apr v 52, No 4 325-30 1 fig & 2 pls.

As the authors point out little is known about the chemical and immunological properties of human malaria parasites, largely on account of the scarcity of material for study. During the recent war concentrates of parasites were prepared from heavily infected human blood by the method of differential centrifugation and by the use of an unsymmetrical magnetic field, which acts on the haematin and related malarial pigments. The antigens were prepared in an attempt to terminate relapses in chronic benign tertian malaria by vaccination of patients for use in prophylaxis, and for studies on the immunological properties of the parasites themselves. In the first method, in which all operations were carried out in the cold with aseptic precautions the separated red cells were washed in formalized saline lysed in chilled water saturated with carbon dioxide and the dissolved haemoglobin was removed after the solid particles had settled. By centrifugation at suitable speeds the leucocytes and stromata of red cells were removed in turn. Several washings with a dilute merthiolate solution removed formalin from the final product. In the case of blood infected with *P. vivax* the best results were obtained when large pigmented forms were present and 15-20 hours were required to deal with a 500 ml. sample.

The second method of separation, which is of academic rather than practical interest was based on the observation of previous workers that Kupffer cells loaded with ferric oxide could be separated from tissue cells in a magnetic field. The present authors found that the pigment of infected cells behaved differently in a magnetic field from the haemoglobin of the normal red cells and that parasitized cells in small volumes of blood could be concentrated by this means. An unsymmetrical magnetic field was obtained by the use of one pole-piece in the form of a cube the other being wedge-shaped. A cell containing 20 ml. of citrated, parasitized blood mixed with 10 ml. of 0.3 per cent. merthiolate in

saline was moulded around the thin edge of the wedge-shaped pole-piece and exposed to an intense magnetic field. Pigmented parasites were drawn towards the edge of the pole-piece and formed a thin brown streak on the wall of the cell. Convection currents were avoided by cooling with a fan and the blood was so diluted that red cells settled in 6-12 hours. The brown streak containing also some red cells was separated along with the supernatant fluid and centrifuged. In the case of blood infected with *P. malariae* 20 per cent of the parasitized cells were recovered by this means with a 140-fold concentration. In the case of *P. vivax* the recovery was 25 per cent with a 15-fold concentration.

J D Fulton

ROMEO VIANONTE J M Los anophelinos de la Isla de Gran Canaria. [The Anophelines of the Island of Grand Canary] *Rev Sanidad e Hig Pùblica* 1946 May v 20 No 5 449-55 17 figs. (15 4 coloured on 5 pls.)

During an investigation of malaria in the island of Grand Canary [see this *Bulletin* 1946 v 43 283] the author examined 123 adult specimens of anopheline mosquitoes of which 96 were *Anopheles (Myzomyia) hispaniola* and 27 were *A. (Myzomyia) sergenti* the figures suggest a predominance of the former species as was noted by CHRISTOPHERS (*Indian J Med Res* 1929 v 17 518). The mosquitoes were caught in the following places — Barranco de Arguineguin Barranco de Ayagayres Telde Santa Lucía de Tirajana and Tejada.

The distinguishing characters of these two species are described and figured.

J F Corson

LUPASCU G Su alcune variazioni delle uova di *Anopheles maculipennis* var *labranchiae* [Some Variations in the Eggs of *A. m. labranchiae*] *Riv di Parasiti* Rome 1941 June v 5 No 2, 121-5 7 figs. [10 refs.]

CORRADETTI A. Le conoscenze sulla distribuzione delle specie anofeliche nell Africa Orientale Italiana. [The Distribution of *Anopheles* in Italian East Africa.] *Riv di Biol Colon* Rome. 1940 Dec. v 3 No. 8, 419-29 [27 refs.]

ROZEBOOM, L. E. & KNIGHT K L. The *punctulatus* Complex of *Anopheles* (Diptera: Culicidae) *J Parasitology* 1946 Apr v 32 No 2 95-131 7 pls. [34 refs.]

This paper reports interesting results and is an excellent example of the kind of investigation that is required to elucidate the relationships of the very closely related but distinguishable groups of mosquitoes which the practical culicidologist in the past has tended to designate as varieties of some well known species.

The authors believe that there are four good species of *Anopheles* specimens of which would before 1939 have been lumped together either as *Anopheles punctulatus* Dönitz or *Anopheles punctulatus* var *moluccensis* Swellengrebel & Swellengrebel de Graaf. It has already been pointed out by KNIGHT & FARNER [this *Bulletin* 1945 v 42 688] that the form to which the name *moluccensis* applies was previously described by Laveran as *farauti* in 1902, and this name must therefore have priority. The four species are as follows — *A. punctulatus* Dönitz (= *punctulatus* of recent authors) *A. farauti* Laveran (= var *moluccensis* of recent authors) *A. koliensis* Owen [this *Bulletin* 1946 v 43 6] described from Guadalcanal and considered by the authors of the present paper to be the same as the intermediate forms (between

*punctulatus* and *farauti*) from New Guinea. A clous Roxeboom and Knight, a new species described by the authors in the present paper from a single female reared from a larva taken near Humbolt Bay, Hollandia.

The authors conclusions are based on biometrical data derived from the examination of series of specimens many with associated larval and pupal pelts and many bred from known females. They admit that they have not carried out all the cross-breeding experiments required to prove that the "intermediate forms" to which the name *holoseris* applies, are not hybrids, but this test was handicapped by the fact that females of *farauti* would not feed in the laboratory, the cross between *punctulatus* male and *farauti* female was therefore impossible under the conditions of their experiments. No hybrids were obtained when *punctulatus* females were given blood-meals and opportunities to mate with *farauti* males though these females, on being given the opportunity to mate with males of their own species did so at once and produced fertile eggs.

John Smart

DULANEY Anna D & WATSON R. B. Complement Fixation in Relapsing *Plasmodium vivax* Malaria. *Amer J Trop Med* 1945 Nov v 25 No 6 473-80 1 fig

These observations carried out at the Kennedy General Hospital U.S.A. relate to 394 patients suffering from relapsing *P. vivax* infections acquired in the Pacific war areas. All the patients were ambulatory except for brief periods during malaria attacks all were free from syphilis. The first group of 133 patients were studied during a six months period on them 287 coincident complement fixation tests and blood film examinations were made. On the second group of 261 patients 6,220 complement fixation tests were carried out.

The antigen used was prepared from pooled *P. knowlesi* parasites of monkeys [COGGESWELL and EATON this *Bulletin* 1939 v 36 404 DULANEY STRATMAN THOMAS and WARR, *ibid* 1943 v 40 11] Saline extracts of the dried parasites were used for all tests in the first group and a quarter of the tests in the second group. A phosphate buffer extract was used for the remaining tests [DULANEY and MORRISON this *Bulletin* 1945 v 42 352]

The results show that the complement fixation test is more sensitive than blood examination in detecting persistent subclinical infections (all the patients had received suppressive atabrin treatment). In the 6,507 coincident examinations there were 4,007 positive reactions 62 per cent but only 854 positive blood films 13 per cent.

The patients could be classified into serological groups: the positive pattern (continued positive) the negative pattern (continued negative) and the changing pattern group. Eighty-eight per cent of the positive pattern group relapsed as compared with 42 per cent of the negative pattern group. 79 per cent of the changing pattern group relapsed. series of positive tests at some time were recorded for all these patients.

In cases of relapse the complement fixation to blood film ratio on the day of attack was 0.7:1 after three days the ratio was 16:1 and after 6 days 80:1.

A series of negative complement fixation reactions with negative blood films over a sufficiently long period suggests the possibility of clinical cure. this period is more than six months.

A conservative attitude toward the test is recommended, an attitude which recognizes its limitations but appreciates the possibilities of its correct use.

Norman White

TUMULTY P A. NICHOLS E SINGEWALD M L & LIDZ T An Investigation of the Effects of Recurrent Malaria. An Organic and Psychological Analysis of 50 Soldiers. *Medicine* 1946 Feb v 25 No 1 17-75 11 charts. [42 refs]

The object of this study of 50 soldiers who had suffered an average of 10 recurrent attacks of *P vivax* malaria was to determine what organic alterations the malaria might have produced and the relative importance of organic and psychological factors in the production of the symptoms displayed by these men

The soldiers six at a time were admitted to a small separate ward in an Army General Hospital in the Pacific area and each was studied during a period of 7 days. Forty three of them were receiving suppressive therapy at the time of the study. 40 with atabrin 3 with quinine. The examination of each was very complete. Detailed medical social and psychiatric histories complete physical examination complete blood study including fragility test urine and stool examinations serological test for syphilis kidney function tests liver function tests tests for adrenal cortical insufficiency basal metabolic rate electrocardiogram teleroentgenogram of the chest special ophthalmological and psychiatric examinations intelligence tests and selected tests to measure certain phases of fatigue. The technique employed in carrying out these tests is described and the results are recorded in detail. A complete summary of this long report is not possible here.

There was no evidence in these patients that numerous attacks of chronic, recurrent *P vivax* malaria caused damage or dysfunction of the organ systems other than the debility from which they suffered. All had been healthy young adults who had been exposed to reinfections for only six months and their attacks of malaria had been treated early and adequately. In nearly all there had been loss of weight and they were easily fatigued. Thirty-six patients had never complained of headache before the malaria. 26 of these developed chronic headache. Exertional dyspnoea was a common symptom. Anorexia and insomnia were complained of by 40 per cent of the patients.

An analysis of the symptoms led to the conclusion that malaria was the prime factor in their production but the individual's adjustment to the malaria and concurrent situational factors contributed to the development perpetuation and intensification of symptoms. Once the symptoms had become fully developed the soldier was of little value to the army but if his morale remained satisfactory he was usually capable of remaining useful. Emphasis needs to be placed upon the handling of the person rather than simply of his malaria. Soldiers who have adjusted poorly in civilian and military life and to overseas service are likely to make a poor adjustment to malaria and to become incapacitated rapidly. Soldiers who develop chronic symptoms early in the course of the disease anorexia indigestion and insomnia should be removed from units where marked physical exertion is required. Their retention is harmful to themselves and to the malarial morale of their units. Minimal hospitalization reduced the tendency towards the development of neurotic patterns.

Norman White

COOK C D & HOFFBAUER F W Liver Functional Impairment in Therapeutic Malaria with particular reference to the Unsuccessful Use of Methionine as a Protective Agent. *J Lab & Clin Med* 1946 Jan. v 31 No 1 56-64 4 figs [23 refs.]

Impairment of liver function has frequently been observed in patients undergoing malaria therapy. The observations described were designed to

determine what protection, if any against such impairment is afforded by the addition of methionine to a general hospital diet.

Twelve patients suffering from neuro-syphilis were inoculated with citrated blood containing *P. vivax* intravenously in 11 cases intramuscularly in one. The plan of the therapy was to maintain fever of over 103°F for a total of 50 hours seven to eleven paroxysms. None of the patients had previously had malaria and none had a history of jaundice or infective hepatitis. In no case was there any evidence of hepatic disease at the time of admission.

All twelve patients were studied with regard to liver function before during and after malaria therapy. The four laboratory tests used were cephalin-cholesterol flocculation, quantitative serum bilirubin the quantitative Ehrlich reaction and the bromosulphalein test. Six of the twelve patients received 8 g. of methionine a day by mouth. All the patients were on a general hospital diet.

There was some evidence of disturbed liver function attributable to the malaria in all twelve patients. There was no evidence that methionine lessened that disturbance in any way. In ten patients functional abnormalities of the liver continued from one to three days after the termination of the malaria.

Norman White

DE MELLO J. P. Malaria in Pregnancy. *East African Med J.* 1946 Jan. v 23 No 1 25-7

HANZLIK P. J. & CUTTING C. C. Clinical Trials with Quinine-Epinephrine Intravenously. *J Amer Med. Ass.* 1945 Dec 29 v 129 No 18 1241-3

The investigation recorded was carried out to determine the safety of intravenous injection of quinine, as commonly used in the treatment of cerebral malaria and the safety and value of epinephrine in preventing the circulatory depression to which intravenous quinine gives rise.

Intravenous injections of quinine-epinephrine were given to seven patients suffering from diseases other than malaria three of whom were in coma from various drug intoxications. Fleeting circulatory stimulation was observed, chiefly an increase in heart rate. The blood pressure was moderately though variably and temporarily increased in four patients. The comas were unaffected.

The authors conclude that quinine-epinephrine intravenously is a safe initial treatment for patients with cerebral malaria. The dosage recommended is 0.5 gm. of quinine hydrochloride or dihydrochloride (or 0.66 gm. quinine bisulphate) and 1 mgm. of epinephrine in 250 cc. of isotonic sodium chloride solution injected in not less than 30 minutes. Not more than two or three such injections, properly spaced should be given within 24 hours.

Norman White

FLOCH, H. Le traitement économique du paludisme par la "quinine activée." [Economic Treatment of Malaria with "Activated Quinine."] *Bull. Soc. Path. Exot.* 1945 v 38 Nos 11/12, 327-41 3 figs. [11 refs.]

The necessity of economizing limited stocks of quinine prompted the use of adjuvants to reinforce its antimalarial action. Preliminary trials led to the adoption of the following prescription —

Quinine hydrochloride	20 gm.
Resorcin	5 gm.
Methylene blue	0.5 gm.
Normal salt solution	250 cc.

After filtration through paper the solution is put up in 2 cc. ampoules, which are then autoclaved for half an-hour at 115-120°C. Each ampoule

contains 16 cgm of quinine hydrochloride and 4 cgm. of resorcin. The treatment consists of two intramuscular injections a day, each of two ampoules for six days. For a time all patients suffering from malaria admitted to the Cayenne General Hospital French Guiana were treated in this way. Clinical notes of nine such cases are given; they included both *P. vivax* and *P. falciparum* infections. The results were uniformly satisfactory. The author considers the results to be comparable to those obtained with three or four times larger doses of quinine without the adjuvants. The mixture can be given intravenously. There were no signs of intolerance.

Norman H kite

TRAGER W BANG F B & HAIRSTON N G. Relation of Plasma Level of Atebrin to Morphology and Motility of *Plasmodium vivax*. *Proc Soc Exper Biol & Med.* 1945 Nov \ 60 No. 2 257-8.

When a single dose of atebrin of 200 mgm. is administered intramuscularly to a patient infected with *P. vivax* at the time of the peak of concentration of the drug in the blood which occurs within an hour of its injection, it is found that most of the larger amoeboid forms of the parasite have lost their motility and show a clumping of the pigment. Some hours later when the atebrin level in the blood has fallen many of the parasites will have recovered their motility and redispersed their pigment. It would seem in view of this recovery after a single dose of atebrin that when malaria is treated by intramuscular injection there is a need for repeated doses. After oral administration of quinine giving plasma concentrations of 6 to 10 mgm. per litre there was no loss of motility and no clumping of pigment within the first three hours. C M Henry

MAEGRAITH B G ADAMS A R D KING J D TOTTEY V M RIGBY D J & SLADDEN R A. Paludrine in the Treatment of Malaria. *Brit Med J* 1946 June 15 903-5 1 chart.

The authors' treatment of benign and malignant tertian malaria with paludrine has already been reviewed [this *Bulletin* 1946 v 43 402]. Their present summary is as follows:—

Paludrine is a colourless slightly bitter drug belonging to a class of chemical compound not previously known to have antimalarial activity. Unlike most other antimalarial drugs it has been found to have an action on the exo-erythrocytic forms of the parasites in *P. gallinaceum* avian malaria.

It has been used successfully in the treatment of benign tertian malaria (both in relapses and in delayed primary attacks) and in acute attacks of malignant tertian malaria (both primary cases and relapses).

It has a very wide therapeutic range of activity. Doses of 10 to 750 mg. and of 50 to 600 mg. twice daily for 14 days have been used successfully in the treatment of benign and malignant tertian malaria respectively. No serious toxic side-effects have been observed with such dosages although occasional nausea and vomiting may occur at dosages of 500 mg. or more twice daily.

The administration of single doses of 50 100 200 300 and 400 mg. will produce clinical cure of relapsing and delayed primary cases of benign tertian malaria. Similar effects have been obtained with single doses of 400 mg. mepacrine.

Twice-daily dosage regimes for 14 days have no greater effect on the relapse rate of benign tertian malaria than full courses of mepacrine. The administration of one dose of 100 mg. weekly after treatment of the acute attack with a single dose of 50 to 400 mg. has so far been found to keep the patient free from relapses. The effect of this therapy over a period of six months is being investigated.

J D Fulton

KING E. J. WOOTTON L. D. P. & GILCHRIST Margaret Estimation of Paludrine in Blood. *Lancet* 1946 June 15 888-7 1 fig

The level of paludrine in the blood during the ordinary course of treatment varies between 10 and 100  $\mu\text{gm}$ . per 100 ml. SPINKS & TOTTEY [this *Bulletin* 1946 v 43 400] developed a method for estimation of paludrine in blood, plasma and tissues, which depends on hydrolysis, followed by diazotization and coupling to give an azo dye. As little as 0.2  $\mu\text{gm}$ . could be estimated in solution in the ordinary way and it was possible to increase the sensitivity of the method by the use of special apparatus. The present authors have used an alternative method based on that described originally by BRODIE and UDEYFRIEND [*J Biol Chem* 1945 v 158 705] and later by MARSHALL and ROGERS [this *Bulletin* 1946 v 43 89] which is simple and rapid, and depends on laking of an acid dye. After extraction of paludrine from whole blood by a benzene-ethanol mixture brom-thymol blue buffered at pH 7 is added. Complete combination takes place between the base and brom-thymol blue within 5 minutes to give a product soluble in benzene, while excess of the dye remains in the aqueous phase. Instead of recovering the coupled dye from the benzene layer by shaking with alkali the authors have, for simplicity, estimated the decrease in brom-thymol blue of the aqueous phase, after making it alkaline so as to develop the deep blue of the dissociated indicator. For measuring optical densities a photoelectric colorimeter is of value and great care regarding cleanliness of apparatus and purity of reagents is recommended. The results of estimation of paludrine by the present method and that of the original authors were in good agreement  
J D Fulton.

INDIAN MED GAZ. 1945 Oct. v 80 No 10 517 Paludrine-M.4888. [Editorial.]

In this Editorial note attention is called to the paper by DAS GUPTA, LOWE and CHAKRAVARTI [this *Bulletin* 1946 v 43 298] in which the compound M.3349 prepared by Imperial Chemical Industries was referred to as Paludrine. The name Paludrine however is now applied exclusively to the later compound produced by the same firm and given the number M.4888. The two compounds differ very considerably in antimalarial activity and in toxicity.

The paper by Das Gupta *et al* is probably the only publication in which M.3349 has been referred to as Paludrine and the name Paludrine is now reserved for M.4888.

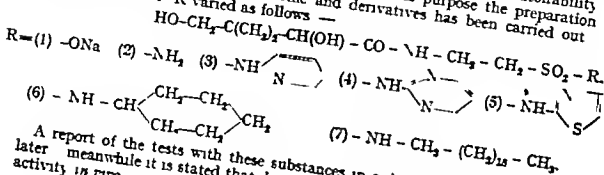
Charles Wilcocks.

CURD F H S & ROSE F L. The Discovery of Paludrine. Reprinted from *Chemistry & Industry* 1946 Feb 16 No 7 75-7

CURD F H S & ROSE F L. DAVIS, M I. HULL, R. LOVELL, B J., OPEXSHAW H T. PAYMAN L C & TODD A R. RAINSON C G. OWEN E. C. TURY G A P. RICHARDSON D N. Synthetic Antimalarials. Part I. Some Derivatives of Arylamino and Aryl Substituted Pyrrolidines [CURD & ROSE] *J Chem Soc* 1946 May 343-51. Part II. 2-Substituted-Anilino-4-Aminoalkylamino-6-Methylpyrrolidines CURD DAVIS & ROSE] *Ibid* 351-7. Part III. Some Derivatives of Meso- and Di-Alkylpyrrolidines [HULL, LOVELL, OPEXSHAW, PAYMAN & TODD] *Ibid* 357-62. Part IV. 2-Phenylguanidino-4-Aminoalkylamino-6-Methylpyrrolidines CURD & ROSE] *Ibid* 363-8. Part V. 2-Naphthylamino-4-Aminoalkylamino-6-Methylpyrrolidines [CURD RAINSON & ROSE] *Ibid* 368-70. Part VI. Some 4-Arylamino-2-Aminoalkylamino-6-Methylpyrrolidines [CURD DAVIS OWEN ROSE & TURY]. *Ibid* 370-78. Part VII. 2-Arylamino-4-Dialkylaminoalkylamino-6-Methylpyrrolidines. Variation of Substituents in the 5- and the 6-Position [CURD RICHARDSON & ROSE]. *Ibid*. 378-84.

MEAD J F RAPPORT M. M. SENEAR, A. E. MAYNARD J T & KOEFLI J B The Synthesis of Potential Antimalarials. Derivatives of Pantoyltaurine *J Biol Chem* 1946 May 163 No 2 465-73 [12 refs]

The views of FIELDS [*Lancet* 1940 May 25 955] that drugs could limit the growth of bacteria by competing with an essential metabolite of the bacterial cell have received confirmation by other workers. Certain sulphonamides are active against malaria parasites *in vitro* perhaps by virtue of a similar effect. The present authors have applied the known facts to the synthesis of possible antimalarials. While there is little information at present available on the nature of essential metabolites of malaria parasites the *in vitro* experiments of TRAGER this *Bulletin* 1943 40 675] indicated that pantothenic acid is a growth factor for *P. lophurae*. Several inhibitors of pantothenic acid metabolism by bacteria are known and this fact suggested to the authors the desirability of testing them for antimalarial activity. For this purpose the preparation of optically active *d*-pantoyltaurine and derivatives has been carried out in compounds 1-7 R varied as follows —



A report of the tests with these substances in avian malaria will be given later meanwhile it is stated that *d*-pantoyltaurine (2) has shown definite activity *in vitro* J D Fulton

SPECTOR S HAVILAND J W & COGGESHALL, L T The Ineffectiveness of Intensive Mapharsen, Bismuth and Carbarsone as Curative Drugs for Chronic Malaria. *Amer J Trop Med* 1945 Nov 25 No 6 463-7 [12 refs]

The reasons that prompted the investigations here recorded were the failure of all drugs hitherto tried to cure a large number of men suffering from chronic relapsing *P. vivax* malaria acquired in the Pacific war area, many of whom are entering the fourth year since infection. The fact that malaria recurrences ceased in a group of eight syphilis patients who were receiving a 26-week course of mapharsen therapy and the desire to decide beyond doubt whether therapeutically effective arsenic compounds in maximum tolerated doses could eliminate this type of malaria, and if not to recommend strongly against their further use.

Four groups of patients were selected. Group I consisted of 15 men each of whom received, during an acute relapse of malaria atebryn, 3.2 gm. over a seven-day period and mapharsen 0.06 gm. intravenously thrice weekly, till each had received 20 mgm. per kilogram of body weight. In Group II nine men were treated with mapharsen and bismuth seven of them were luteic. The bismuth subsalicylate was given intramuscularly. Seven men in this group received a minimum of 30 mgm. mapharsen per kilogram of body weight. In Group III 48 patients received carbarsone a pentavalent arsenical by mouth. Ten men received carbarsone alone 0.5 gm. twice daily for 7 days. the remaining 38 received atebryn in addition 0.2 gm. twice daily for 7 days. Group IV the control group consisted of 94 patients who were treated with atebryn 0.2 gm. thrice daily for one day then twice daily for 6 days a total dose of 3 gm.



Within a month of the termination of treatment 7 of the 15 patients in Group I had both parasitic and clinical relapses—by the end of the third month only three had remained parasitically and clinically free of malaria. In Group II only four had remained free of a parasitic or clinical relapse at the end of 3 months. In Group III carbarsone alone caused the disappearance of parasites from the blood in all but one case but in four parasitaemia reappeared within 10 days—in the 3-month period all had had parasitic relapses but only 3 of the 10 had had clinical attacks. Among the 39 men who received carbarsone and atabrin at the end of 3 months there had been 24 parasitic relapses (63 per cent.) and 14 clinical relapses (37 per cent.). The control group of 94 patients who had received atabrin alone had in the same period 66 per cent. parasitic and 47 per cent. clinical relapses.

The conclusion is that arsenical preparations such as mapharsen and carbarsone are not indicated in the treatment of acute or chronic malaria.

Norman White.

GILLETTE H. P. S. The Progress of Malaria Control Measures in Trinidad and Tobago with special references to County St. David. *Caribbean Med J* 1945 v 7 Nos. 4, 5 & 6 212-30

In a malaria survey of Trinidad and Tobago (this *Bulletin* 1944 v 41 445-7) 13 species of anophelines were found in Trinidad and three in Tobago. Since then another anopheline—*A. parsonsi*—has been reported from Trinidad. *A. aquasalis* and *A. bellator* are the chief vectors of malaria in Trinidad, and *A. aquasalis* in Tobago. *A. aquasalis* readily enters human habitations—the time of greatest invasion is from 6.30 to 8.0 p.m.—a second less intense invasion occurring from 3 to 5 a.m. Its range of flight from breeding places may extend to three miles and possibly to five miles at certain seasons of the year. For purposes of larval control however a zone of one mile radius round the area to be protected gives good results. After biting, *A. aquasalis* does not remain long in the house. Animal barriers are of value in maintaining a low *aquasalis* malaria rate. Among permanent control measures, good results have been obtained by the construction of a culvert with a beak, or sea head, designed to keep the mouths of small streams open and by automatic flushing syphons. Paving ditches and levelling and filling have yielded excellent results in some places. The destruction of bromeliads in which *A. bellator* breeds by spraying with a one-half per cent. solution of copper sulphate continues to give good results.

A detailed account is given of the control measures carried out from 1941 to 1944 in the County of St. David, which forms the north-east corner of Trinidad. The success achieved is remarkable. St. David is now the least malarious county in the colony—formerly it was the most malarious.

Norman White.

MAGDOON E. H. Drainage for Health in the Caribbean Area.

This book is reviewed on p. 877

BOVARTICK, Marianna R. LINDSAY ANN & HELLERMAN L. Metabolism of the Malarial Parasite, with reference particularly to the Action of Antimalarial Agents. I. Preparation and Properties of *Plasmodium lophurae* separated from the Red Cells of Duck Blood by means of Saponin. *J Biol Chem* 1946 May v 163 No. 2, 523-33. [21 refs.]

These respiration studies with *P. lophurae* were undertaken to obtain information on the mode of action of antimalarials. Previous studies by others

on similar lines and with various species of malarial parasites had so far failed to elucidate the mechanism of inhibition of respiration by drugs. In order to eliminate the influence on metabolism of the red cell the parasites were freed from the latter by a modification of the saponin method of CHRISTOPHERS & FULTON (this *Bulletin* 1940 v 37 190). The present authors indicate that the factors of chief importance in this method are the concentration of saponin used and the temperature at which parasites are incubated with this substance. Respiration measurements showed that the oxygen uptake of erythrocyte-free parasites was sometimes 70 per cent. of that of the original parasitized cells but varied more widely under different conditions of storage and experimental temperatures than the latter. This comparative instability of separated parasites could not be diminished by any treatment. The partial loss of respiratory activity was attributed to destruction of the duck red cells which themselves respire actively and lose their activity through the action of saponin. The reciprocal action of the metabolic activities on one another of red cell and parasite host must also be considered. Special buffer solutions were used in respiration measurements and for washing red cells the glucose usually present in the latter being omitted when other substrates were being studied.

The rate of oxygen uptake by intact parasitized cells varied with the stage of development of the parasite as shown by other workers (this *Bulletin* 1942 v 39 397 and 742 1943 v 40 674 1945 v 42 448). With glucose as substrate the R.Q. of the separated parasites varied between 0.7 and 1.0. Only when lactate or pyruvate was used as substrate was their oxygen consumption similar to that observed when glucose was used. The inhibition of respiration by cyanide was complete but was less marked when azide was used. The inhibition could be counteracted to some extent by cresyl blue and other reversible dyes the former by itself inhibiting normal respiration to some degree. This increase in respiratory activity brought about by cresyl blue was believed to be due to its action on the red cell. An investigation of the inhibition of oxygen uptake by these separated parasites through the action of quinine or atabrin in presence of various substrates showed that it only occurred to any extent at the relatively high concentration of 0.001 M in each case and varied but little with the nature of the substrate. Cyanide-cresyl blue respiration was unaffected by these two drugs.

J D Fulton

BOVARNICK Marianna R. LINDSAY Ann & HELLERMAN L. Metabolism of the Malarial Parasite, with reference particularly to the Action of Antimalarial Agents. II. Atabrine (Quinacrine) Inhibition of Glucose Oxidation in Parasites Initially depleted of Substrate. Reversal by Adenylic Acid. *J Biol Chem* 1946 May v 163 No 2 535-51 [21 refs]

In Part I above the authors noted that a relatively high concentration (0.001 M) of atabrin (quinacrine mepacrine) was required to cause marked inhibition of oxygen consumption by *P. lophurae*. Inhibition did occur however at much lower concentrations in the case of parasites previously depleted of substrate, in which case there was a well defined lag period before the oxidation of added glucose began which was reduced when lactate pyruvate fumarate or succinate were used as substrates. The measurements of glucose utilized and oxygen consumed during this period were in agreement. The nature of this inhibition by atabrin has now been investigated.

Erythrocyte-free parasites were obtained and depleted of oxidizable substrates by washing and shaking for a period of 100 minutes at 37°C. in suitable buffer medium. The parasites apparently suffered damage proportional to the length of the substrate free period. It was found that the induction period, before oxidation of added glucose begins could be reduced by the addition of

certain other substrates during the period of depletion, or along with glucose at the end of that period. The inhibition of oxygen uptake by atebirin in substrate-depleted cells was most marked when glucose was the substrate added and caused an 80-90 per cent inhibition of recovery in contrast to a 20 per cent inhibition in parasites not previously depleted of glucose. The marked effect on inhibition could be partially prevented by adenosine triphosphate (ATP) and adenylic acid (adenosine-5-phosphate) as well as by succinate and fumarate. These agents did not however appear to prevent cell damage. The inhibitory effect of atebirin under these conditions varied to some extent with the sample of blood used and may have been due to the removal of the free drug by solid constituents of the suspension. When washed parasitized cells were used which could not be wholly depleted of substrate like the separated parasites a similar sensitivity to atebirin was not apparent. A number of other drugs including quinine and plasmoquine, behaved like atebirin at low concentrations in preventing recovery of respiration in substrate-depleted cells. The specificity of action of adenylic acid in antagonizing the actions of atebirin led to an examination of phosphorus exchanges in cells and medium. It is probable that ATP and adenylic acid exert their effect in the speeding up of glucose oxidation by aiding the phosphorylation of this substance. Owing possibly to its impermeability 1-6 diphosphofructose was without effect on the parasites. FULTON (this Bulletin 1940 v 37 509) found that *P. knowlesi* was unable to oxidize hexose di- or mono-phosphate. It is possible that the action of atebirin is due to interference with some phosphorylation reactions which are necessary before glucose can be utilized.

J. D. Fulton

MARSHALL E. K. JR. LITCHFIELD J. T. JR. & WHITE H. J. The Antimalarial Action in Ducks of certain Sulfanilamide Derivatives. *J. Pharm. & Exper. Therap.* 1946 Mar v 88 No 3, 273-9

It was previously shown by the authors (this Bulletin 1943 v 40 223) that sulphonamides are active against *P. lophurae* infections in ducks when the blood concentration of these substances is maintained at a suitable level. Their action is antagonized by *p*-aminobenzoic acid. In the present investigation, and with similar methods the previous observations have been extended. White Peking ducklings weighing about 100 gm. were infected with  $100 \times 10^6$  red cells parasitized with *P. lophurae* which produced a peak of parasitaemia on the 6th day. Similarly  $50 \times 10^6$  red cells infected with *P. calhemerium* gave a peak on the 4th-5th day. The drug was administered in the diet, and treatment which was given over a period of 5-10 days was started 24 hours before infection. The birds were kept in light and in darkness, alternately for 6-hour periods. The percentage reduction in parasitized cells at the time of peak-infection in controls was used as a measure of drug activity. On account of the wide variations in the degree of parasitization of the experimental birds the geometric mean of individual values was used for assessing the value for a group. Quinine was used as the standard drug and the ratio of its minimal effective dose (producing a significant reduction in parasitaemia) to that for other drugs served to measure their relative activity. On this basis an evaluation of slightly active drugs is possible.

By this test sulphadiazine was found to possess high activity relative to quinine in *P. lophurae* infections. The percentage of parasitized cells could not however be reduced below 1-2 per cent (compared with a 70 per cent infection in the controls at the peak period on the 6th day) whatever the dosage of sulphadiazine used. Quinine was much more effective in this respect probably on account of its more rapid action, for the effect of the two

drugs was similar when the peak of infection occurred on the 10th day and a graded response relative to dosage was then obtained. By using *P. cathe-merium* infections in the same hosts a marked difference in species susceptibility to sulphonamides was noted. Those in clinical use were not so effective against *P. cathe-merium* as against *P. lothurae*. The activity of two halogen substituted sulphonamides was about equal in both infections and was considerably greater in *P. cathe-merium* than that of the sulphonamides in common use. Judging by the fact that the halogen derivatives were antagonized to a much lesser degree than the other sulphonamides by  $\beta$ -aminobenzoic acid their mode of action may be different

J. D. Fulton

MISSIROLI, A. Sullo sviluppo dei parassiti malarigeni [On the Development of Malaria Parasites] *Riv. di Parasit.* Rome 1940 June v 4 No 2, 69-78  
2 text figs. & 27 figs. on 3 pls (2 coloured)

## TRYPANOSOMIASIS

BURTT, E. Incubation of Tsetse Pupae Increased Transmission-Rate of *Trypanosoma rhodesiense* in *Glossina morsitans* *Ann. Trop. Med. & Parasit.* 1946 Apr v 40 No 1 18-23 3 figs [18 refs.]

Most previous work on the transmissibility of *Trypanosoma rhodesiense* has stressed the fact that the vertebrate host and the parasite have important bearings on the frequency with which the tsetse vectors become infected. In this paper experiments are described which show that the temperature to which the pupae of tsetse flies are exposed may profoundly influence the infectibility of the flies by trypanosomes—this newly-discovered factor in the transmission of trypanosomes must be taken into consideration in regard to past and present work both in the field and the laboratory.

Pupae of *Glossina morsitans* collected in the field were hatched out in the laboratory some after keeping at laboratory temperatures and others in an incubator at 30°C (86°F). Unfortunately the author has not given the laboratory temperatures to which the pupae were exposed and it is to be hoped that he will do so but they were evidently below the incubation temperature as a comparatively large number of the experiments were made during the cooler season from June to August. The flies were removed from the incubator within 24 hours of emergence and thereafter kept like the others under normal laboratory conditions. The results are shown in tables and charts.

Of 21 068 flies which emerged from pupae kept at laboratory temperatures and were fed on animals—sheep reedbuck Thomson's gazelle or monkey (*Cercopithecus* sp.)—infected with *T. rhodesiense* 7 127 lived long enough for complete development of the trypanosomes in them, and 296 (4.2 per cent) showed infection of the salivary glands while of 9,335 flies which emerged from incubated pupae 3,352 lived long enough for complete development of the trypanosomes and 408 (12.2 per cent) showed infection of the salivary glands.

The infection rate of flies from incubated pupae varied according to whether they fed on infected sheep reedbuck gazelle or monkey but the difference was more marked with monkeys and Thomson's gazelle than with reedbuck or sheep. The results were all based on isolation of infective flies since the modified dissection methods of Lloyd and Johnson [this *Bulletin* 1934 v 31 215 1937 v 34 113] used at first was found to be unreliable.

Transmissibility seemed to be further raised if incubation of the pupae was prolonged. The time taken for the completion of the cycle of *T. rhodesiense* in the fly was significantly shorter in those from incubated pupae than in those from normal pupae.

In all the experiments (110) with batches of flies from incubated pupae transmission resulted, though many were done in the cooler season but failure resulted in many of the experiments made with batches of flies from pupae kept at laboratory temperatures. No difference in longevity was observed between the two groups of flies.

VANDERPLANK (unpublished) in 1943 working independently of the author obtained similar results with *T. congolense* in both *G. morsitans* and *G. swynnertoni*.

A further question which arises from this work is whether cooling of the pupae would produce flies more resistant to infection with trypanosomes.

The practical importance of the results is discussed, particularly as it may influence the seasonal incidence of trypanosomiasis. Kenneth Mellanby

BURTT E. The Sex Ratio of Infected Flies found in Transmission-Experiments with *Glossina morsitans* and *Trypanosoma rhodesiense*. *Ann Trop Med & Parasit* 1946 Apr v 40 No. 1 74-8 [15 refs.]

In these experiments at Tinde laboratory about twice as many male as female *Glossina morsitans* developed salivary gland infections. This was true whether the pupae from which the flies emerged had or had not been incubated [see above] and whether the infection was derived from sheep, reedbuck, gazelle or monkey. The male and female flies emerged in equal proportions from both incubated and unincubated pupae but in both cases there was a considerably higher death rate among female than male flies throughout their maintenance in Bruce fly boxes but not when towards the end of the experiments they were kept singly in bottles after having fed. Other workers have shown that both in the laboratory and in nature female flies tend to survive slightly better than male flies. It therefore appears possible that at Tinde a greater proportion of potentially susceptible (to infection) female flies were being weeded out by early death than males and that this might be responsible for the difference in the rates of infection in males and females.

DRUX [this *Bulletin* 1930 v 27 847] found in experiments with *G. palpalis* that approximately equal numbers of male and female flies developed salivary gland infections. Female *G. palpalis* survived significantly better in his experiments than female *G. morsitans* did at Tinde and Burtt suggests that *G. palpalis* withstands mass confinement better than *G. morsitans*.

As the infection rate of tsetse flies is usually low, the proportion in which the sexes survive in experiments should approximate to that occurring in nature. As this was not the case at Tinde the question of the relative infectibility of the sexes remains unanswered and experiments with flies kept singly in bottles are needed. It is a question of practical importance both for the correct interpretation of experimental results and of what takes place in nature.

Kenneth Mellanby

DE AZEVEDO J. F. CAMBOURXAC F. J. C. & PIATO M. R. A doença do sono na Guiné em 1944 e observações sobre Ofídios, Culicídeos e *Phlebotomus* da Colónia. [Sleeping Sickness in (Portuguese) Guinea in 1944 and Observations on the Local Snakes, Culex and *Phlebotomus*]. *An Inst Med Trop* Lisbon. 1945 Dec. v 2 7-47 21 figs. on 10 pls. & 3 folding maps. English summary (4 lines).

The information given in this article is so condensed that it might almost be designated in itself an abstract. In November 1943 a Commission was set

up to investigate the prevalence of sleeping sickness in Portuguese Guinea and to devise methods of prevention because shortly before several severe cases of the disease had been observed among Europeans. The Commission started its work on 3rd January 1944 and returned on 23rd February having spent 50 days in the Colony. The amount of work attempted and accomplished during this brief period is astounding. They examined the natives domestic and wild animals caught and dissected specimens of *Glossina* investigated the clinical aspects of the disease and its influence on the general mortality in this paper they discuss the outlook and prophylaxis as regards the European and the native and report on a study of the snakes and insect fauna. As if this were not enough they were also asked to undertake in their stride as it were and as matters of secondary interest a study of the prevalence and extent of yellow fever and to collect evidence on the endemicity of malaria in the country.

The natives were collected in 48 places on an average about 200 in each in all 8543 were examined 397 of them had enlarged glands and were therefore suspected of trypanosomiasis and 61 of the glands were positive on puncture. The authors collected 3930 specimens of *Glossina* and dissected 1103 the proboscis salivary glands or intestine of any found infected were inoculated into laboratory animals. Ninety five per cent. (3720 of the 3930 collected) were *G. palpalis* 146 (9.7 per cent.) were *G. submorsulans* and the remainder 64 were *G. longipalpis*. Only 0.8 per cent. of the 1103 dissected showed infection by polymorphic trypanosomes of the *T. gambiense* group (salivary glands were infected in 6 (0.54 per cent.)). No domestic animals horses cattle or sheep were found to harbour trypanosomes infective for man. A gazelle was found with a trypanosome of the *T. gambiense* group.

The effect of infection with trypanosomes on the general mortality is said to be slight and the authors think that the strain of *T. gambiense* is one of low pathogenicity and is peculiar to the district. Individuals might be found heavily infected but nevertheless show practically no clinical signs. But, though the course of disease is long and apparently mild, fatal cases do occur. Comparing the present findings with those of Professor SEQUEIRA in 1932 they conclude that the disease has undoubtedly increased and spread. Until the reason for this extension is known, it is difficult in fact not possible to foretell the future in this respect. Prophylaxis consists in avoiding the fly belts as far as possible in travelling in the early morning or after dark, when the *Glossina* is less active and in the preventive use of Bayer 205 for those who have to enter the infected zones. It would, they suggest be well to set up a permanent mission to study and deal with the disease in Portuguese Guinea.

During their sleeping-sickness work, 10 species of snakes were caught one was a python seven were Aglyphae or Opisthoglyphae and so non poisonous two Viperidae were poisonous *Causus rhombatus* and *Bitis aridans*. The collecting of diptera was not included in the Commission's terms of reference but say the authors they did not lose the opportunity of examining them. Among their catches were *A. gambiae* *A. coustani* var. *tenebrosus* a *Culex* which could transmit filaria to man and dogs and certain protozoa parasitic in birds and two species of *Phlebotomus* namely *P. signatipennis* and *P. jallas*.  
H. Harold Scott.

DE AZEVEDO J. F. CAMBOURNAC, F. J. C. & PRINCE M. R. Sobre a infestação por tripanosomas das Glossinas da Guiné [Infestation of *Glossina* by Trypanosomes in Spanish Guinea.] *An. Inst. Med. Trop. Lisbon*. 1945 Dec. v. 2. 49-66 3 figs. English summary.

DEWEY H. M. & WORMALL, A. Studies on Suramin (Antrypol Bayer 203). 5  
The Combination of the Drug with the Plasma and other Proteins. *Biochem J* 1946 v 40 No 1 119-24 1 fig [10 refs.]

This paper describes a continuation of work previously reported in this *Bulletin* 1939 v 36 688 1940 v 37 19. In this earlier work it had been shown that much of the Suramin found in the serum is in combination with proteins. The methods used to estimate Suramin do not differentiate between unchanged Suramin and degradation products or other substances which produce aromatic amines when hydrolysed by acid. Suramin combines with proteins quickly (in a few minutes). Much of the Suramin bound to proteins of human serum remained bound even after long extraction with methanol or aqueous ethanol. The amount bound varied in different experiments, but in one a fully extracted preparation still contained 5 per cent of Suramin (i.e. 3.5 mol. Suramin per 1 mol. protein of mol. wt. 100,000). The original concentration of Suramin in these mixtures of serum and Suramin was 1-2 ml. Suramin solution (0.2-0.6 per cent) in 20 ml. serum [i.e. of the order of 0.01 to 1 per cent.]. In some experiments with gelatin and casein from 70 to 80 per cent of the Suramin originally present became bound to these substances, but appreciably less was fixed by the serum protein. When Suramin is hydrolysed by acid the absorption of the degradation products by serum protein is much less than that of the original Suramin and the absorbed material can easily be removed by extraction with methanol. When hydrolysed Suramin is injected intravenously into rabbits almost all of it disappears from the blood in 6 hours. When unchanged Suramin is injected considerable amounts persist in the blood for 90 days. Unhydrolysed Suramin is retained in the tissues of treated rabbits for many days. Hydrolysed Suramin is not retained in this way.

[There is some evidence that Suramin also combines with trypanosomes since trypanosomes which have been exposed to Suramin and then washed are no longer infective for animals, although they remain motile *in vitro* for over 24 hours at 37°C. see HAWKING this *Bulletin* 1939 v 36 742.] F. Hawking

DIAS E. Acenta de 254 casos de doença de Chagas comprovadas em Minas Gerais. [Observations on 254 Cases of Chagas's Disease in Minas Gerais.] *Brasil Medico* 1946 Feb 2 & 9 v 60 Nos. 5, 6 41-4

These brief notes refer to 254 cases of Chagas's disease seen in the States of Minas Gerais up to 26th December 1945. Of the total, 118 were males 136 females. 168 were whites 40 were negroes and 46 half-castes. The ages of those infected are given showing that no age is exempt. 33 were under 5 years, 50 between 6 and 10 years, 52 between 11 and 15, 27 between 16 and 20, 30 in the third decade, 28 and 20 in the fourth and fifth respectively. 16 were over 50 years of age. The primary lesion was on an eyelid in 38 cases among 57 studied elsewhere on the head in 6 (ears, lips, etc.) on arm or leg in 10 and one on the chest. The month of infection is noted in 47 but this is of little value where the total is so small. Suffice it to say that from September to February the cases numbered 5, 6, 6, 6, 7 and 8. In March and May there were 3 each, in April, July and August one, in June none.

The diagnosis was made by xenodiagnosis in 163, by serological reactions (chiefly complement fixation, using a culture of the trypanosome as antigen) in 44, by blood examination in 40 and histologically post mortem in two.

There were 13 fatal cases among the total 254. Electrocardiographic tracings were made in 207. 110 were normal, 97 abnormal. A V block in 42, first grade in 30, second grade in 3 and total in 9 of the right ramus in 33. As regards residence 105 were living in the town of Bambul, 131 in the municipality.

but outside the town and 18 further afield Details of the places of residence in the different suburbs 95 cases in all are given but are of local interest only  
H. Harold Scott

DIAS E & FERREIRA L. B Doença de chagas em São João Batista do Glória Oeste de Minas Gerais. Estudo dos transmissores e breve relato de cinco casos [Chagas's Disease in São João Batista do Glória, Minas Gerais Study of the Vectors and a Short Account of Five Cases] *Brasil Medico* 1946 Mar 2 & 9 v 60 Nos. 11 12 & 13 83-5 [11 refs.]

TORREALBA F J Investigaciones sobre enfermedad de Chagas en el Estado Guárico-Venezuela. [Study of Chagas's Disease in Guárico State Venezuela] *Gac Med de Caracas* 1945 Sept-Dec v 53 Nos 18/24 168-74 2 figs

Though other causes of myocardial mischief exist in the rural population such as malaria schistosomiasis syphilis ankylostomiasis and alcoholism the commonest is infection by *T. cruzi*. The author quotes abundantly from the literature of the last 12 years instancing cases of sudden death from this cause such as the young baseball player apparently in excellent health running to a base and dropping dead another dying suddenly while working in a maize field Prior to 1935 such deaths were usually ascribed to syphilitic myocarditis Examination of persons perhaps showing no signs of disease clinically may reveal enlarged hearts arrhythmia extrasystoles intermittency and bradycardia as low as 23 per minute Cases are quoted in which four brothers were affected in this way another family with three brothers and two uncles It must not be thought that sudden and early death is invariable A case is referred to where a patient showed heart block and was proved by xenodiagnosis in 1939 to be infected but still carries on his work though with an intermittent and irregular pulse Details are given of six patients in the rural district with signs of myocarditis tested by xenodiagnostic methods. Three of these gave positive results and one of the negative gave 3-plus Wassermann and Kahn reactions  
H. Harold Scott

LAZZA S Sobre la pretendida relación de enfermedad de Chagas y bocio y cretinismo endémico A propósito de profilaxia del bocio [On the Supposed Relationship between Chagas's Disease and Endemic Goitre and Cretinism. The Prophylaxis of Goitre.] *Revista d Circolo Medico de Mendoza* 1945 Sept Oct Nov & Dec Nos 69/70 7 pp.

[This article rather stresses what is now well known that infection with *T. cruzi* is not the cause of the thyroid conditions observed in districts where Chagas's disease also persists.] The author states that the idea of *T. cruzi* infection being the cause of endemic goitre and cretinism ought now to be dropped that there is practically nothing to support it. He then quotes various workers CARINI PEREIRA COVTO SERPA BERCOVITZ GONZALEZ FLORIANI and others who have promulgated the error Professor LAZZA then speaks of one case a child of 7 months dying after a period of marasmus from syphilis and infected with *T. cruzi* in whom leishmanial forms of the parasite were found in all the organs and tissues the thyroid among them. Since then among 1,200 cases of Chagas's disease the authors and his co-workers have not seen a single case of goitre consequent on *T. cruzi* infection.

H. Harold Scott



## LEISHMANIASIS

ARCHETTI, I. Distribuzione e diffusione delle leishmaniosi nell'Africa Orientale Italiana. [Distribution and Spread of Leishmaniasis in Italian East Africa.] *Riv di Biol Colon* Rome, 1940 Dec., v 3 No. 6, 401-18, 1 map. [Numerous refs.]

NAJERA, L. Observaciones sobre la ecología de los *Phlebotomus* en su fase larvaria principalmente. [Observations on the Ecology of *Phlebotomus*, principally on Larvae.] Reprinted from *Rev Ibérica de Parasitología* 1946 Jan-Apr v 6 139-58 19 figs [29 refs.]

Reviewing general information on the food materials of the larvae of *Phlebotomus* spp. the author emphasizes particularly the observations of PARROT [see this *Bulletin* 1933 v 30 308] and his co-workers that the larvae of some species will feed in captivity on the dried leaves of various trees. Such species include *P. papatasi*, *P. perniciosus*, *P. langeroni* var. *longicuspis*, *P. arisi*, *P. sergenti*, *P. parroti* and, of Central African species *P. schouti*. He considers this phytophagy a true biological character and points out that it is of considerable interest in explaining the general limitation of *Phlebotomus* to rural and suburban districts.

In laboratory cultures the author found that larvae eat filter paper with voracity when it is impregnated with liquids carrying nutritive organic substances in solution. His breeding technique was as follows —

Females caught in bedrooms, with fresh or partially digested blood meals were put up in glass tubes of 5 cm. length and 2 cm. diameter. The bottoms of the tubes were lightly packed with cotton wool separated from the rest of the tube by filter paper disks cut accurately to fit the lumen and pushed down in contact with the wool, which was soaked in water. The mouths of the tubes were closed by a double layer of gauze and all the tubes were stacked vertically in petri dishes in a chamber of nearly 100 per cent relative humidity. Eggs were laid on the filter paper, some on the wall of the tube and were easy to examine and count with only low magnifications. About 70 per cent. of females oviposited and 20 per cent. deposited all the eggs contained in their ovaries. After oviposition the females usually died. Rearing of the hatched larvae was carried out in small unglazed baked-clay pots containing a layer of paste made from guinea-pig faeces over a layer of plaster. They were sunk in wet sand in a closed humid chamber.

Left after hatching in the tubes the larvae developed to the second, sometimes the third, instar and migrated downwards into the cotton wool but they did not attack the filter paper. They did however attack the filter paper when it was put in the pots with the nutritive medium. Apparently therefore the cellulose of the paper is only eaten when it is impregnated with nutritive liquids. This behaviour has so far been observed only in *P. papatasi* and *P. perniciosus*.

The author discusses these phenomena of phytophagy and papyrophagy in relation to the pre- and post-war distribution of *Phlebotomus* in Madrid. Before the war they were confined to the periphery of the city and the vicinities of parks and gardens. Since 1940 they have increased and are abundant in other localities in the middle of the city. Although to superficial observation there is little alteration of the city from its pre-war condition, there are scattered throughout it many bombed sites which have not been rebuilt. Such sites are often unwallied and are used frequently as rubbish dumps or public latrines. A selection of photographs and a list of such sites are given but the city was not examined systematically. Between 1942 and

1944 148 soil samples from 33 sites were examined and 14 were found to contain *Phlebotomus* larvae. Almost all the positive findings were made in the months June to September. He points out the danger of the introduction of infantile kala azar into cities under these conditions and recommends that bombed sites should be enclosed and all organic debris therein destroyed.

W H R Lumsden.

SEN GUPTA P C & CHAKRAVARTY V K. Penicillin in Cancrum Oris complicating Kala-Azar. *Indian Med Gaz* 1945 Nov v 80 No 11 542-5 2 figs. on pl.

It is well known that cancrum oris is one of the most fatal complications of kala azar giving a mortality rate of at least 50 per cent in spite of vigorous treatment with sulphonamides and pentnucleotide in addition to specific treatment for the leishmania infection. This unsatisfactory result has led the authors to test the effect of penicillin and in this paper they report on the treatment of six cases—five in children 2 to 10 years of age and one in an adult. Penicillin was administered intramuscularly or intravenously every three hours for about a week in doses of 10 000 units while local applications of penicillin solution containing 500 units per cc. were made for three weeks. In one case penicillin was administered as a lozenge. In addition specific treatment with pentavalent antimonials was carried out while general supportive measures were undertaken. Under the penicillin treatment the necrotic process was quite unlike that seen in the cases that recovered in previous years. It was rapidly checked and did not continue to extend while separation of sloughs occurred in all but one of the cases in 72 hours. All the patients recovered and the end results as regards scarring and deformity were fairly satisfactory. In one or two of the cases the course of penicillin was repeated to expedite healing. It is concluded that the system of treatment adopted in the cases described is likely to meet with better success than the treatments which were previously adopted.

C M Wenyon

CHAKRAVARTY K. C. The Treatment of Kala-Azar with Sodium Antimony Gluconate (Stibatin). Further Observations on the Treatment of Thirty-Two Cases. *Indian Med Gaz.* 1945 Oct v 80 No 10 507-11 8 charts [10 refs.]

In an earlier paper [this *Bulletin* 1945 v 42 17] the author with BURKE reported upon the treatment of 21 cases of kala azar with sodium antimony gluconate or antimony hexonate (stibatin of Glaxo Laboratories). In all these cases there was immediate clinical cure but the follow up was too short to justify any statement as to permanency of cure. The author of the present paper has followed up these 21 cases for six months. 18 had remained quite healthy and can be considered cured, while 3 had relapsed. He also reports on the treatment of 32 other cases of kala azar in patients varying in age from under 10 to over 40. In children under 15 the total quantity administered was ten times the age in cc. or 1 cc. for each year of age multiplied by 10. For older patients the standard total dose is 1.5 cc. (or 30 mgm. of the antimony compound) for each pound of body weight divided into 10 daily doses. In patients of such high weight that the total dose works out at over 200 cc. the number of injections may be increased. The drug is remarkably non toxic for in the cases treated there was an immediate reaction of palpitation in only one case while in two cases albuminuria developed after four and seven injections. This albuminuria disappeared when the course was interrupted and it did not recur when treatment was resumed. The 32 cases were followed up

for six months when it was found that only two had relapsed. The author concludes that the drug is specific in the treatment of kala azar and on account of its low toxicity and ease of administration owing to its being supplied in solution ready for injection it is specially useful when mass treatment is required.  
C M Wenyon.

SEN GUPTA P C & CHAKRAVARTY N K. The Treatment of Kala-Azar with Sodium Antimony- $\gamma$ -Glucosate Preliminary Observations. *Indian Med Gaz* 1945 Nov v 80 No 11 560-64 [18 refs]

In this paper the authors report on the treatment of 50 cases of kala azar in India, with sodium antimony glucosate in doses higher than those previously employed. The procedure adopted was to give daily intramuscular injection for 10 to 12 days of 15 to 20 cc in the case of adults or 6 to 15 cc. in the case of children. It was found that there was little irritation the patient being able to walk home within 15 to 20 minutes after the injection. An analysis of the actual doses employed in the 50 cases gave a total dosage as follows Children 3.7 cc. adolescents 2.7 cc. adults 2.1 cc. per pound of body weight. In seven patients the course had to be repeated. The immediate result of this treatment was very satisfactory as there was a clinical cure in 48 of the 50 cases. One of the failures was a case which proved resistant to all treatments and the other was in a case complicated by agranulocytosis.

In addition to the cases of kala azar two of post-kala azar dermal leishmaniasis in adults were treated by two courses of 10 or 11 injections at a week's interval. In both there was early and marked improvement.

All the cases treated are being followed up to determine if relapses do or do not occur  
C M Wenyon

CAMPOS J A Intradermo-reacção de Montenegro precoce [Accelerated Montenegro Reaction.] *Arquivos de Hyg e Saúde Pública* São Paulo 1945 Mar v 10 No 23 43-6 English summary (9 lines)

After the intracutaneous injection of leishmania antigen in the application of the Montenegro test for cutaneous leishmaniasis, an anaemic swelling is at first produced which later in positive cases becomes a red papule. In a varying number of cases the reaction is indefinite. The authors have tested in a series of eleven cases the effect of cupping the initial swelling for 3 to 17 minutes. The result has been the earlier development of the positive reaction which increases in intensity while the indefinite reactions about which there may have been doubts become definitely positive. Completely negative cases are uninfluenced.

C M Wenyon

## FEVERS OF THE TYPHUS GROUP

CRAIGIE J Application and Control of Ethyl-Ether Water Interface Effects to the Separation of Rickettsias from Yolk Sac Suspensions. *Canadian J Res. Sect. E. Med. Sci.* 1945 June v 23 No 3 104-14 4 figs. [15 refs]

This paper consists of two parts the first which deals with the use of ethyl ether in the purification of rickettsial suspensions made from infected yolk sacs was issued as a confidential document in February 1942 the second is a supplementary note submitted for publication in January 1945.

Two methods of purifying the triturated yolk-sac suspensions by ether are described. Method A is stated in the supplementary note to remain the

method of choice for the small-scale preparation of pure suspensions of rickettsiae for use in serological investigations whereas Method B which was formerly used in the preparation of vaccines is said to have been replaced later by a method of processing crude yolk sac rickettsial suspensions at pH 7.0

In Method A the triturated suspension is centrifuged the total sediment is suspended in saline buffered with phosphate at pH 7.0 and then emulsified with ethyl ether the rickettsiae are recovered from the aqueous fraction that separates as the unstable emulsion breaks down

In Method B preliminary centrifugation is omitted the separation of the aqueous fraction is controlled by the addition of acetate buffer to the crude triturated yolk sac suspension and there is a maximum yield of rickettsiae which are afterwards treated with ethyl ether

The principles involved and the somewhat complicated technique employed in both methods are described but they cannot usefully be summarized.

The use of ethyl ether in the purification of suspensions of viruses and certain bacteria is discussed in the supplementary note the ether is said to have three useful properties it acts as a bactericidal agent a lipid solvent and a remover of tissue impurities from virus suspensions

John W D Megaw

BRUMPT L. C & MACLOUF A. C. Un cas de typhus exanthématique à incubation prolongée et apparemment déclenché par un pneumothorax thérapeutique [A Case of Exanthematic Typhus with Prolonged Incubation, and apparently Precipitated by an Artificial Pneumothorax Operation] *Bull et Mém. Soc. Méd. Hôp. de Paris* 1946 Nos. 13/14 205-8.

An attack of typhus fever occurred in a Polish patient who had previously been exposed for a long time to the risk of infection in Buchenwald Camp. Forty-one days before the onset he came into close contact with infected persons and ten days later he was thoroughly disinfested with DDT after having discarded all his prison clothes retaining only his mantle. He reached France 25 days before the onset on arriving in Paris 22 days before the onset he burned all his clothes. Since his disinfestation 31 days before the onset he had not been exposed to any known risk of infection.

Artificial pneumothorax was induced seven days before the onset the authors suggest that this may have been responsible for lighting up a latent infection of the reticulo-endothelial system. They consider it unlikely that infection was caused by inhalation of dried infected louse faeces. They mention that the maximum incubation period of louse-borne typhus is stated by DANIELOPOULU as 20 days and by NICOLLE as 22 days also that in murine typhus caused by living vaccine the incubation period may be as long as 25 days.

John W D Megaw

PROC. ROY. SOC. MED. 1946 Feb. v. 39 No. 4 165-8 (Sect. of Exper. Med. & Therap. 15-18) Discussion on D.D.T. [CAMERON G. R. CHALKE H. D. HILL, K. R. CASE, R. A. M. HELLIER, F. F. HACKETT C. J. CHESTERMAN C. C.]

CHALKE describes the conditions in Naples in the autumn of 1943 which led to an outbreak of typhus in November. During the last five weeks of that year the weekly numbers of cases were 36, 22, 45, 36 and 133. In 1944 up to 9th January the incidence increased to 340 a week then dropped dramatically to half this number remained stationary for three weeks after which it fell to 40 early in February then gradually declined there being a total of 1,600 cases.

The main preventive measure applied in the early part of the epidemic was an intensive search for cases and the treatment of all contacts with insecticide

applied in powder form by means of mechanical blowers. Up to the end of 1943 only about 10 per cent. of the dustings were done with DDT the remainder being done with British or American preparations "AL 63" and "MYL," neither of which then contained DDT. From January 1 all dusting was done with 10 per cent DDT in talc and apparently at about the same time the mass dusting of large numbers of people replaced the dusting of known contacts. Chalke concludes that taking into account the incubation period and the fact that few cases were notified before the fourth or fifth day the initial control of the epidemic was brought about as a result of intensive case searching and the ringing of contacts with barriers of insecticide at a time when DDT was used only to a very limited extent. The epidemic, checked in this way was finally ended by the large scale use of DDT.

Chalke also describes the method of use of DDT solutions in the destruction of adult anopheline mosquitoes in Italy in 1944.

HELLIER, describing conditions in Northern Europe mentions a dermatitis associated with purpura amongst soldiers wearing shirts impregnated with DDT and concludes that it was not due to DDT as such but to some associated factor. Presumably as a result of wearing treated shirts, lousiness was very rare among troops in France, Belgium and Holland, though their use did not seem to prevent the occurrence of scabies and pediculosis pubis both of which became common in Belgium and Holland. G Macdonald

WOODWARD T. E., PHILIP C. B. & LORANGER, G. L. Endemic Typhus in Manila, Philippine Islands. Report of Cases and Identification of the Murine Rickettsial Agent in Domestic Rats by Complement Fixation. *J. Infect. Dis.* 1946 Mar-Apr v 78, No 2 167-72, 1 fig. [10 refs.]

A detailed description is given of an attack of typhus fever in an American soldier which occurred near Manila. *Proteus OX19* was agglutinated at a titre of 1-2,500 the reaction with *Pr OXA* was negative. The murine complement fixation titre rose to 1-384 the epidemic titre was 1-6.

Two other cases were seen in the Manila area, and one in Mindanao though these were not closely studied the serological reactions were of the same type.

Sera of 100 rats (89 of which were *Rattus norvegicus*) caught in Manila, were tested by murine complement-fixation reactions. 18 were positive at titres ranging from 1-12 to 1-192. Only one of the rats reacted with *Proteus OX19* at a titre of 1-80 ten reacted with *Pr OXA* but at low titres of 1-20 or 1-40.

*Yenopsylla cheopis* in limited numbers, and the mite *Neoschoengastia indica* large numbers were found on the rats.

Suspensions of the brains of two rats and of the mites from another rat, were inoculated into guinea-pigs with negative results. These three rats had given positive reactions with the complement-fixation test. A guinea-pig was inoculated with blood from one of the patients also with negative results.

John W. D. Meyer

STUART B. M. & PULLEN R. L. Endemic (Murine) Typhus Fever. Clinical Observations of 180 Cases. *Ann Intern Med.* 1945 Oct v 23 No. 4 520-36 5 figs. [32 refs.]

During the 16 years 1829-1944 180 cases of endemic (murine) typhus were seen in a hospital in New Orleans. Only 21 of the cases occurred during the first ten years of the period. In 1839 there were 16 cases and in the successive five years the figures were —19 44 14 34 and 32. The authors believe that even when allowance is made for better diagnosis there was a real increase in the prevalence of the disease.

The disease was most prevalent in summer and early autumn only two cases occurred in the month of March then the incidence steadily increased, reaching its peak in August in which 49 cases occurred during the five months June to October there were 128 cases the remaining 52 cases were distributed among the other seven months of the year

The average age of the patients was 34.6 years there were no deaths A macular rash was seen in 81.4 per cent of the 129 white patients and in 19.6 per cent of the negro patients it extended to the face in three cases and to the palms in two

The clinical features and Weil Felix responses as described do not appear to differ in any important respect from those commonly observed in louse-borne typhus of corresponding severity

The leucocyte picture was none too characteristic but there was usually a slight degree of leucopenia during the first week and the average total count increased progressively from the fourth day reaching a maximum of 11 000 per cmm by the 15th day Biopsy of the macular lesions was found helpful in diagnosis excised macules were fixed in Regaud's fluid and stained by the Giemsa method.

Although most of the patients were admitted after more than one week's illness the presumptive diagnosis on admission was usually wrong it was typhus fever in only one fourth of the cases

MORALES F H Report of a Case of Typhus Fever *John W D Megaw*  
Rico 1946 Feb v 38 No 2 68-9 *Bol Asoc Med de Puerto*

The author describes an interesting case of typhus fever (presumably of murine type) which occurred in Porto Rico in July 1945

The patient had been vaccinated with a Wilmington murine strain of vacc sac vaccine about four months previously On July 3 he noticed a purulent discharge from one ear On July 7 he was bitten by a guinea pig suffering from an acute febrile and orchitic reaction after inoculation with typhus rickettsiae On July 12 he was put on a course of penicillin injections for the staphylococcal infection of the ear the treatment was continued till July 22, by which date he had received nearly two million units of the drug On July 20 he began to suffer from a mild attack of typhus fever which lasted 10 days The Weil Felix (O\19) reaction was positive in rising titre which reached 1-3,200 by the 10th day

The attack was attributed probably to the bite of the guinea pig its mildness was thought to have been due to previous inoculation or the penicillin treatment or both combined.

DINGLE DINE Mary J WILLIS Carolyn & HARRELL, G T High Protein Diets  
In Therapy of Rocky Mountain Spotted Fever *John W D Megaw*  
1946 May v 22 No 5 389-91 *J Amer Dietetic Ass*

Eight children suffering from Rocky Mountain spotted fever were kept on a diet rich in protein carbohydrate and all the vitamins but low in fats When the patients could not be persuaded to take a full standard diet by the mouth gavage was employed.

Several children actually gained weight during the illness and the authors believe that convalescence was shortened by the generous diet

No details of the effects of the treatment on protein metabolism are given these are being reported elsewhere.

*John W D Megaw*

## YELLOW FEVER.

LAGOS NIGERIA. Annual Report of the Yellow Fever Research Institute 1945. 110 typed pp 12 photographs 5 maps 12 figs. & 1 folding chart.

The Annual Report of this Institute for 1944 was reviewed in this Bulletin 1945 v 42 800. The Institute was reopened for full work towards the end of 1943 after an interval of almost 10 years during which it had practically been closed and during 1944 most of the work done was preliminary to the projected full-scale activities which were envisaged for the future. During 1945 the staff was built up and in the last quarter the Institute functioned with a full staff for the first time. New buildings were constructed, but it was not possible to erect permanent structures.

One of the first enquiries made was an investigation of the distribution of yellow fever in Nigeria. Only one case had been found since 1942. Protection tests were carried out on blood from the people especially children from various parts of the country and the results showed 16 per cent. of positive tests. Immune children were found relatively frequently in areas in which the disease has been reported during the last 10 years but the most interesting discovery was that, according to this evidence there had been a recent outbreak of appreciable proportions within sight of Lagos. Moreover three monkeys shot in the vicinity all gave strongly positive tests. Lagos itself, however appears to have escaped, and the explanation of this is not certain. It may be that the relatively low density of *Aedes aegypti* would not permit an extensive outbreak, or that the strain of *Aedes aegypti* present is poor in carrying power. The information however indicates repeated widespread yellow fever outbreaks among the Africans throughout Nigeria south of latitude 10° N. It is calculated that there must have been many thousands if not several hundreds of thousands of cases in the past 15 years yet recognition of the disease in the Africans is exceptional. Part of the explanation no doubt is that the medical service is inevitably thinly spread over the country but more important is the fact that in the African yellow fever tends to be a mild disease. This is not true of Europeans and the absence of large outbreaks in Europeans must be attributed to preventive measures, of which vaccination is the chief. As a background to the human disease there lies the still almost unknown subject of yellow fever in monkeys. Evidence has been collected which points to these animals as the reservoir but the subject has not yet sufficiently been studied. Investigations are now being made.

The experimental work done at the Institute included a study of the susceptibility of mice of different ages to subcutaneous injection of yellow fever virus. In the course of this study it was found that there is marked change in the blood-brain barrier. This change can be detected at the 7th day of life and develops with great rapidity to the 10th day. In other words before the 7th day a relatively small dose of virus given subcutaneously will kill the mice after the 10th day the dose must be many thousands of times greater to achieve the same result. This phenomenon is probably due to the fact that mice are born while still in a relatively embryonic state. It seems not to be true of guinea-pigs which are more mature at birth. The practical outcome of this and similar work in South America is that for the mouse-protection test, animals less than 8 days old should be used, and small amounts of virus. In this way weakly positive sera which with grosser tests would be missed, can be detected.

The susceptibility of mice to the yellow fever virus has been very thoroughly investigated. Two strains of mice are kept at the Institute one from Lagos (originally from Hamburg) and the other from Entebbe (originally from Rio

de Janeiro) In each strain there exists a fraction which for all practical purposes is completely resistant to the virus in the Lagos strain about 7 per cent and in the Entebbe strain about 1 per cent of the mice appear to be refractory These qualities of susceptibility or non susceptibility appear to be genetic and work has now been put in hand whereby by selective breeding it is hoped to rear a susceptible strain from the Entebbe strain. An interesting fact has been observed namely that mammary carcinoma develops very frequently in the Entebbe strain but not in the Lagos strain

On the basis of the finding of susceptible strains of mice the argument is developed that the same phenomenon probably occurs in other wild animals in nature and that certain strains of mosquitoes (for instance *Aedes aegypti*) may not possess the faculty of transmission of the virus to the same extent as other strains For instance, *Galago demidovi* (the smallest of the bush-babies) was found to be somewhat refractory to yellow fever virus though the larger species *G. senegalensis* was found by Smithburn in East Africa to be highly susceptible Investigations into the vector efficiency of varieties of *Aedes aegypti* are being made and the evidence is becoming more conclusive that populations of the same taxonomic group may differ markedly in their response to virus and that these variations may exist in the same area at different times Inevitably epidemiology develops genetic facets for complete understanding [This important subject of inherited characters has a very wide application not only to the susceptibility of hosts to an infecting organism, but also probably to the infective power of different strains of the infecting organism. It is discussed in relation to trypanosomes by CORSON (this *Bulletin* 1946 v 43 169-176) and the work of LURIE on susceptibility of in-bred strains of rabbits to the tubercle bacillus is also much to the point (see *Bulletin of Hygiene* 1941 v 16 670 1945 v 20 313) The development of similar enquiries may lead to extensive changes in the conceptions of epidemiology.]

Other laboratory investigations included the estimation of the effect of temperature on the virus-antibody reaction tests of susceptibility of local guinea-pigs the effect of defibrination and of sodium citrate on virus in blood (these are not deleterious to the virus) and the effect of variations in the time of injection of starch into the brain in relation to intraperitoneal injection of virus (simultaneous injection of each appears, on the whole, to be the best procedure)

It is well known that the development of a viscerotomy service is essential to the efficiency of a research and control scheme for yellow fever The beginnings of such a service have now been made in Nigeria. Difficulties are expected, especially among the Mohammedans of the north but elsewhere it seems to be quite possible that viscerotomy will be successfully carried out

Some work was carried out on other diseases in which the suspicion was aroused that they may have been due to viruses other than that of yellow fever but without definite result. An account is given of the distribution of yellow fever vaccine during the year

Charles Wilcocks

HEATON C. E. Yellow Fever in New York City *Bull. Med. Library Ass.* 1946 Apr v 34 No. 2, 67-78 [38 refs.]

A historical account.

FRANKMAN G. Epidemiology and Incubation Period of Jaundice following Yellow Fever Vaccination. *Amer. J. Trop. Med.* 1946 Jan., v 26 No. 1 15-32, 8 figs. [14 refs.]

An epidemiological study of jaundice following yellow fever vaccination was undertaken at Camp Baker in the south-eastern U.S. About



half of the population of 18 000 was transient moving in and out on a weekly schedule while the other half was permanent and could be more clearly studied. The epidemic coincided in time and duration with the large general epidemic among American troops during 1942. Altogether slightly more than 700 cases or approximately 3.8 per cent. of the total average population at risk, were hospitalized with jaundice. The first six cases occurred sporadically between August 1941 and February 1942 and these patients had not been vaccinated. Three companies were inoculated on December 30th 1941 and during the first week of January 1942 and of these approximately 500 men nine had jaundice during the last 3 weeks of March or roughly 70-80 days later. The three companies were housed in nine barracks holding some 50 men each: no cases occurred in 7 of the barracks, 4 in one and 5 in another: a distribution very unlikely to occur by chance. The bulk of the population was vaccinated between February 23rd and March 9th 1942 and the main epidemic was continuous from May to September with its peak in the last week of June. The personnel first affected belonged to Company A of Regiment Z. Members of this Company had received either YFV lot M1 or M2 during the first week of March while at the same time the rest of the regiment received M2. 13 cases occurred in Company A during May and the first week of June before any occurred in the remainder of the regiment: an event most unlikely to occur by chance. The spatial distribution was also odd, for of the 12 barracks in which Company A was housed 9 had no cases, 1 had 1 case, 1 had 3 cases and 1 had 7. Examples from other units are given of these discrepant events both in space and time.

The average interval of time between vaccination and onset of epidemic jaundice was 12.3 weeks but varied between units from 11 to 15 weeks. The incidence in units appeared to fall in defined waves with an interval of 2 to 4 weeks between their peaks and an average of 3.2 weeks.

It appears therefore that there were two factors interwoven in this epidemiological pattern: namely YFV and the focal grouping of cases. The latter the spatial and temporal grouping of cases of jaundice in certain barracks and units among troops having received common YFV at approximately the same time points towards a communicable disease with an incubation period of 2-4 weeks rather than to one caused by iatrogenic vaccine. A large increase in the attack rate on the unvaccinated population was also observed and it is likely that all the cases of jaundice whether they did or did not receive YFV had a common aetiology. The YFV used on certain Army posts appears to have had the property of predisposing its recipients to the communicable disease referred to as jaundice and this property varied among the several lots of YFV.

[The evidence is set out graphically and the paper is a difficult one either to read or to abstract adequately.]

A Bradford Hill

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## PLAGUE

BHATNAGAR, S. S. & SHRIVASTAVA, D. L. An Experimental Study on Cellular Immunity in *Pasteurella pestis* Infection. *J Hygiene* 1948 May v 44 No. 5 307-13 3 coloured figs. on 1 pl. [20 refs.]

This study relates mainly to the leucocyte picture of the peripheral blood as an index of resistance or immunity. A supravital staining technique was

used with neutral red as the indicator stain. Janus green the mitochondrial stain which is ordinarily used along with neutral red, had to be omitted as the combination of the stains was too toxic for cells in the presence of a bacterial infection. Total leucocyte counts and differential counts were also used. The two test animals were the highly immune Bombay rat and the highly susceptible inbred laboratory mouse. Immunization (passive) or protection was effected by injection of one of the three types of sera known as pure envelope, pure somatic and whole antiplague serum. Of the pure sera it is the envelope type alone which is protective and this was confirmed by the cellular leucocyte response here investigated. Two types of leucocyte or rather three are distinguished the polymorphonuclear (or microphage) and the macrophages (monocyte and clasmatocyte). Clasmatocytes are distinguished from monocytes by their much greater size and were significantly absent during the tests of cellular response in relation to active immunity of susceptible mice. Here the polymorphonuclear leucocyte reacted vigorously at an early stage and it was this cell which appeared to form the first and the last line of defence of the susceptible inbred laboratory mouse. Its steady deterioration cytologically was an index of the downhill course of infection.

It was otherwise with the cellular response to the protective envelope serum where the penetration and segregation in pattern of neutral red was a marked index of immunity. No protective value of polymorph leucocytosis could be demonstrated in either serum treated or non treated white mice. It was the detection of clasmatocytes in the peripheral blood that was found to be an objective observation of great prognostic value and this has to be coupled with observations on the monocytes. The association of monocytes with passive protection was well marked. Their maintenance at high level connoted protection while a significant diminution in their number heralded a fatal termination. An increase or a decrease of neutral red vacuoles in monocytes or clasmatocytes was an indication of degree of functional digestive activity for living particulate material. It was this index which was found both in the case of immunity and susceptibility to show whether the struggle was developing in favour of host or parasite. The test should therefore as the authors contend be valuable for immunological assessment of the value of plague-serum therapy and plague prophylaxis.

W F Harvey

Pozzo Adolfo Peste de Oriente.

This book is reviewed on p 880

## BACILLARY DYSENTERY

BRODIE J COOK R P DRYSDALE Constance F & McINTOSH D G Treatment of Sonne III Bacillary Dysentery and Bacillary Dysentery ("Clinical") with Phthalyl Sulphathiazole *Brit Med J* 1946 June 22 948-50 [10 refs.]

Forty-eight cases of Sonne III dysentery, and 40 cases of clinical dysentery (blood and mucus in the stools but no organism isolated) were treated with phthalyl sulphathiazole at King's Cross Hospital Dundee in the period from August 1944 to June 1945. The dosage is shown in Table 1.

TABLE I.  
Dosage of Phthalyl Sulphathiazole

Age in years	Grammes per day					Total in grammes
	1st	2nd	3rd	4th	5th	
0-2	3	1	1	1	1	7
3-5	3	2	2	2	2	13
5-12	10	3	3	3	3	22
Over 12	15	4	4	4	4	31

The results are compared with those obtained by JAMIESON BRODIE and STIVEN [this *Bulletin* 1944 v 41 754] who treated 100 cases with sulphaguandine 50 with saline aperients and 50 with chalk mixture this comparison is shown in Table III.

TABLE III  
Comparison of Treatments for Bacillary Dysentery

Treatment	No. of cases		Average time in days required for clinical cure		Cases positive bacteriologically in convalescence			
	Sonne III	Total	Sonne III	Total	Sonne III		Total	
					No.	%	No.	%
Aperients	11	50	6.3	6.5	4	36.4	25	50
Chalk	18	50	7.6	8.0	11	61.1	26	52
Sulphaguandine	10	100	4.7	5.0	4	40.0	30	30
Phthalyl sulphathiazole	48	—	8.73	—	10	20.8	—	—

The present results with phthalyl sulphathiazole agreed with those obtained with sulphapyridine by STIVEN [this *Bulletin* 1943 v 40 844] who found that the stools in treated cases remained abnormal for 9 days compared with 20 days in control cases.

The amount of free phthalyl sulphathiazole in faeces blood and urine was estimated and it was shown that a small amount had been absorbed from the alimentary canal.

In vitro experiments showed that phthalyl sulphathiazole exerts a bacteriostatic effect against a number of intestinal organisms. A Flexner strain a Sonne III organism and a strain of *B. coli* were completely inhibited in semi-solid and fluid media containing the drug.

The authors conclude that phthalyl sulphathiazole did not influence the clinical course of Sonne III dysentery but reduced considerably the number of cases bacteriologically positive in convalescence.

J. F. Corson

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

DORMER, B A Pulmonary Amoebiasis. *Proc Transvaal Mine Med Officers Ass* 1945 Nov v 25 No 278 113-27 6 diagrams & 23 pls

In Natal S Africa, acute amoebic dysentery and amoebic hepatitis are very rare in the well fed Europeans although 5 per cent. harbour *E histolytica* they are also very uncommon in the fairly well fed Indian population but they are very common in the Bantus 17 per cent of whom have been shown on a single stool examination to harbour the parasite (three times this number may therefore be assumed to be infected) The incidence of acute and of metastatic *E histolytica* infections in the Bantus has risen steadily since the war especially in the urban areas Tuberculosis and amoebiasis show a strange parallelism in the Africans who are poorly fed and live on a protein-deficient diet. The author postulates that a high carbohydrate (especially maize or rice) and low animal protein diet favours amoebic bowel infection and that a reasonably high protein diet with wheat as the staple carbohydrate does not do so The stools of the African are highly acid indicating a bacterial chemical and physical state of the bowel favourable to amoebiasis while those of the European are alkaline and the conditions are unfavourable to the parasites [No explanation is offered of the low incidence of amoebiasis and its manifestations in the presumably rice-eating Indian community] Epidemic bacillary dysentery is rare in the Natal native and this is due to the acid bowel medium which does not favour the growth of the causative organisms.

Amoebiasis is common in the tropics as high relative humidity leads to longer survival of cysts outside the body and the food habits of the people are conducive to its establishment in them Infection rates on the coast are greater than inland as inland the humidity is less and the temperature lower The author considers that the provision of adequate first-class protein in the diet of the Bantus and the reduction of maize and rice products as the principal source of carbohydrate with replacement by wheat would with proper sanitation and education control the situation. The treatment of the individual essentially consists of dietary rectification with drug treatment as an ancillary where necessary The author then goes on to a discussion of pulmonary amoebiasis illustrating by drawings and X ray photographs cases of direct extension of infection from the liver to the lung and of embolic infection of the lung [The author's conclusion that diet *per se* plays a major part in the infection of the individual does not appear to have been substantiated elsewhere In the Japanese prison camps amoebiasis was not unduly obtrusive when sanitation could be attended to in spite of the inadequate and almost exclusively rice diet Furthermore amoebiasis was very prevalent among well fed troops living on a high protein diet under the unavoidably insanitary fly ridden conditions obtaining for brief periods during active operations. Again while high relative humidity may favour longevity of cysts outside the body high temperatures do not do so and cysts will not withstand ordinary drying whatever the atmospheric humidity Does not a more adequate explanation of the incidence of amoebiasis lie in the personal habits housing and sanitary standards obtaining among the various communities?]

CHAUDHURI R N & RAI CHAUDHURI M N Pulmonary Amoebiasis. *Indian Med Gaz* 1946 Feb v 81 No 2 66-7 3 figs. (1 on pl.)

Amoebiasis of the lung is much more common than is thought but is often undetected, or is misdiagnosed as pulmonary tuberculosis The authors review some of the few published reports of the clinical condition and add to these

two further case reports from the Carmichael Hospital for Tropical Diseases Calcutta. Both patients were Bengali women aged 24 years. In the first case the X-ray appearances were suggestive of tuberculosis but no bacilli were found no *E. histolytica* were recovered from the sputum or stools and emetine injections cured the pain and physical signs in the right chest, the cough, fever and loss of condition for which the patient was admitted. In the second case *E. histolytica* but no tubercle bacilli were found in the sputum and none in the stools on admission to hospital there were fever cough, and blood-stained sputum but no physical signs and again, emetine injections proved specific. Both cases had some leucocytosis that in the first being marked (23,500 per cmm.) and that in the second slight. In each case there was initial aggravation of the symptoms on beginning emetine injections. A R D Adams

WITHERSPOON F G Exfoliative Dermatitis associated with Amoebic Dysentery *Arch Dermat & Syph* 1946 Mar v 53 No. 5 506-7

A case of exfoliative dermatitis with an associated amoebic dysentery is described. On successful treatment of the amoebic infection great improvement in the dermatologic condition occurred. A search of the available literature has revealed no similar case.

CHAPIN S. E. Positive Urine Methylene Blue Test in Amoebic Hepatitis. *J Amer Med Ass* 1946 Apr 20 v 130 No 16 1071-2.

In a case of amoebic hepatitis in a young American Marine the methylene blue test of the urine [see *Bulletin of Hygiene* 1945 v 20 660] was strongly positive and the urine contained a considerable amount of bile. *Entamoeba histolytica* was present in the faeces in large numbers. Treatment with emetine, carbarsone, choline chloride a high protein diet and multivitamin tablets was followed by apparent cure in 3 weeks. The methylene blue test of the urine became negative on the 5th day after the beginning of treatment.

The authors recommend the test as directing attention to the liver in acute inflammations of that organ. J F Corson

CHAUDHURI R. N & RAI CHAUDHURI M N A Case of "Amoeboma." *Indian Med. Gaz* 1946 Mar 81 No 3 138-9 3 figs. on pl.

HARGREAVES W H The Treatment of Amoebiasis with special reference to Chronic Amoebic Dysentery *Quart. J Med* 1946 Jan., v 15 No 57 1-23. '85 refs.]

After a brief account of the distribution, epidemiology and incidence of amoebic dysentery the author reviews in detail the drugs believed to exert some influence on the infection. Emetine is the most effective drug available but alone, it is not often curative. Emetine bismuth iodide is the most efficient basis for combined specific treatment if it is given in a proper form as a powder in gelatin capsules and not in pills or tablets. After stressing the importance of early diagnosis and efficient treatment the author discusses the bewildering number of treatments variously advocated, and the criteria by which their efficacy has been judged. The variations in the claimed successes of various treatments by sundry authors may be attributable to variation in the standards adopted for assessment of cure. The pathology of the infection in the bowel and the symptomatology due to it receive attention at some

length and the author then turns to the refractory cases of amoebic dysentery which arrived in the United Kingdom from the Far Eastern theatres of the late war. Questions of emetine-resistance of variations in virulence of different strains of parasites and of secondary bacterial infection superimposed on the amoebic infection are considered in detail. Hargreaves does not think there is any evidence of the development of emetine fastness by *E. histolytica* and the position in regard to variations in virulence of different strains of the parasite he thinks is far from clear. The available evidence points to differences in susceptibility of the patients rather than to biological differences in the strains of organisms as the cause of variations in severity of the manifestations resultant on the presence of the parasite.

Secondary bacterial infection plays an important part in determining the severity of the colitis and in preventing a satisfactory response to anti amoebic treatment. Successful control of this secondary bacterial infection with penicillin and succinyl sulphathiazole results in markedly more effective action of the amoebicidal drugs and it also may save life in grave cases of superadded bacillary colitis. Chronic cases of amoebic dysentery previously labelled emetine-resistant have been cleared of their infection by standard treatment with EBI and chiniofon enemata after a penicillin and sulphasuxidine course. Only occasionally has more than one course of the standard anti-amoebic treatment been necessary to obtain cure after the bacterial infection has been dealt with although this latter may need more than one course of penicillin and sulphasuxidine to overcome it.

The indications for surgery in amoebiasis and the use of the sigmoidoscope are discussed and the general management of the patient and the author's standards of examination for cure are detailed. That the difficulties in the diagnosis and treatment of amoebiasis were fully realized by the Germans is evident from the fact that they dropped propaganda leaflets containing advice to our troops on the methods of simulating the disease in its refractory form. A copy of one of these is given.

A R D Adams

WANTOCH H G Zur Frage der sogenannten nicht-pathogenen Amöben.  
[So-called Non-pathogenic Amoebae.] *Schweiz. med. Woch.* 1946 Mar  
30 v 76 No 13 280-81

The author from his experiences in Shanghai maintains that the so called non pathogenic amoebae of the human intestine are far from being non-pathogenic for in his experience they are liable to cause various disturbances such as abdominal discomfort or pain diarrhoea or constipation. In no case, however is there real dysentery with blood and mucus in the stools as in the case of *E. histolytica* infections. In most of the cases quoted *E. coli* was the amoeba present and when the infection was eradicated by yatren acetarsol carbarsone or other suitable remedies the symptoms abated.

C M Wenyon

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

WILLIAMSON J & LOURIE E M Therapeutic Action of Different Penicillins  
on *Spirochaeta recurrentis* Infections in Mice *Brit Med J* 1946  
June 1 828-9 [11 refs.]

The authors have compared the therapeutic action of three different preparations of penicillin—(a) The partially purified product as issued for

parenteral injection (b) crystalline penicillin II (c) crystalline penicillin III—on relapsing fever infections in mice.

No significant differences were found between the actions of the partially purified preparations and crystalline penicillin II but penicillin III was substantially less effective.

The present experiments suggest that it is becoming increasingly necessary to investigate the anti-spirochaetal properties of the by-products in the manufacture of penicillin. Since the more easily and more copiously produced forms of penicillin such as penicillin II are more active against infections of *Spirochaeta recurrentis* it is suggested that they may also be more active against *syphilis*. This would be fortunate if substantiated, since this disease requires such a high aggregate dosage.

F Hindle

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE. PUBLICATION No 18 A Symposium on Relapsing Fever in the Americas.

This book is reviewed on p 881

NOBREGA, G. Um caso de sodoku [A Case of Bat Bite Fever] *Brasil Medico*. 1946 Feb. 2 & 9 v 60 Nos. 5/6 35-6 2 figs.

Up to April 1939 Professor DA FONSECA had recorded 14 cases of sodoku in Brazil. Nevertheless, says the author none of the standard text books on tropical medicine contains any reference to the existence of this disease in Brazil [but SITTI mentions South America in the geographical distribution]. The author consequently is anxious to place the present case on record.

The patient was a boy of 11 years and was bitten on the left hypothenar region on 23rd September 1943. The wound bled slightly and was treated with mercurochrome. Four days later the wound became painful and there was a little discharge from it. Six days after the bite he had a bout of fever and the wound continued to be painful. It then healed and cicatrized but during the next 3 weeks he had 5 paroxysms of fever lasting for 48 to 72 hours. They were not ushered in with any rigor or shivering and there was no terminal sweating—the only symptoms were the rise of temperature to 39.4°C., with headache and rapid pulse. The epitrochlear gland was swollen and slight enlargement of the axillary glands was observed. *Ascaris* and ankylostome ova were numerous in the faeces but there was no cosmophilus (4 and 3 per cent. only on two occasions when the total leucocytes were 13,500 and 16,000 per mm.) As the wound had healed no fluid could be obtained from it for examination. Gland puncture was refused, but 15 cc. of blood taken during a febrile paroxysm was inoculated into white rats (camondongos) and these animals 11 days later showed infection by *Spirillum minus*.

H Harold Scott.

## LEPROSY

SCHUJMAN S. Criterio para otorgar el alta hospitalaria a los enfermos de lepra. [Criteria for the Release of Lepor Patients from Hospital.] *Rev Argentina Dermatofilologia* 1945 Dec v 29 No. 4 249-52.

One gathers from the text of this article that the subject of discharge of lepers from hospital was posed as one for discussion at the Third Congress on Leprosy. The term "discharge" is regarded as being of three types (1) Permission to leave hospital on the promise of continuing treatment and attending a dispensary (2) Conditional on coming up periodically for observation

(3) Definitive the patient ceasing treatment and severing all connexion with the Leprosy Department. The present contribution deals with the first of these. It is of epidemiological importance from the points of view of the patient his relatives and associates.

Rules at present are far from uniform. In the Philippines it was the custom to let the patients go from hospital after being for 6 months. bacterially and clinically negative but a large percentage were found to relapse so the time was increased to one year. In Hawaii patients were let out on parole after three negative examinations carried out at intervals of 3 months. At Carville when a patient became negative he was passed on to a special section of the establishment where he was treated and under further control for two years and if at the end of that time he was still negative he received his discharge. In São Paulo they used to be released after being negative for a year but so many were found to relapse that this period was doubled.

In the author's view the decision must depend on several grounds. It is of the utmost importance to note the condition on arrival the type and extent of the disease. Notes on progress must be made frequently and discharge from hospital will depend on the clinical state on admission the number of bacilli then present and on the progress made clinically and bacterially and immunologically and on the treatment which has been adopted. With this proviso he suggests the following as guides.

- (a) Tuberculoid cases with isolated lesions may be allowed to leave after being bacterially negative for 8 months. For those showing reactions the time should be prolonged to a year in those giving a definitely positive Mitsuda test and 1½ years in those giving a weak positive.
- (b) In lepromatous cases we should be more cautious according to the intensity of the process. Those of L1 type should be detained in hospital for two years after they become negative. treatment should be continued during this time and frequent clinical and bacteriological examinations should be made bimonthly for the first year and monthly for the second. For L2 and L3 patients the period should be at least three years and provocative measures should be tried such as the giving of potassium iodide sulphanilamides tuberculin etc. before a case is declared negative.

H Harold Scott

CERBONI E. A. PECORARO V. & RODOLFO MERCAU A. Bases para la reglamentación de las altas de los enfermos de lepra. [Bases for Rules for Discharge of Lepers from Hospital.] Rev Argentina Dermatosisifilologia 1945 Dec. v 29 No 4 253-6

The rules or regulations proposed by the authors are based on those of São Paulo adapted to the South American classification of cases of leprosy and to the present-day ideas on its immunology. A brief sketch of what is done in other countries is given as a preliminary. [These have been noted in the preceding abstract and need not be repeated.] The rules are laid down for the three types mentioned by SCHUJMAN [see above.]

- 1 Release from In-patient Treatment—(1) Within 30 days of admission the patient should be examined and classified in one of the following three categories (a) Lepromatous (b) Non-characteristic, bacteriologically positive (c) Tuberculoid bacteriologically positive.
- (2) When they become bacterially negative. Those of (a) should continue under observation for two years those of (b) who react negatively to immunological tests to be under observation for 12 months those positively reacting for 6 months those of (c) to be kept under observation for 6 months.
- (3) During the period of observation they should undergo a clinical and bacteriological examination (the latter of the skin the nasal mucosa and gland



juice obtained by puncture) every 3 months and a histo-pathological examination every 6 months.

(4) The above being satisfactory an ophthalmological and laryngological examination should be made to exclude any active lesions in these sites.

(5) The patient is then sent, with his clinical history before a medical board. In addition to the history of the case from the time of the patient's admission, information should be furnished regarding his intended place of residence, his means of living and his immediate associates will be under supervision.

(6) A patient so discharged should subject himself for re-examination every 4 months for 2 years and bring a certificate from his doctor that he has been under his constant treatment.

The patient will now come under the category of those —

II *Conditionally discharged* with permission to engage in certain occupations and to suspend treatment with the doctor's consent. The following may come under this heading: Tuberculous cases and the non-characteristic bacterially negative, which have had two years' treatment whose lesions have retrogressed and who show no signs of activity.

Patients conditionally discharged are still under observation by the Board and should be examined every 6 months for 5 years, being treated or suspending treatment at the decision of the medical attendant.

III *Definitive discharge*—Those who have fulfilled the conditions of the previous group—who have been examined every 6 months for 5 years have remained clinically free from symptoms and bacterially negative even after provocative tests as by administration of potassium iodide and any other tests which the Board may require—will be eligible for final discharge.

H. Harold Scott

FIOZ, H. *Atlas a los enfermos de lepra.* [Discharge of Lepers from Hospital.] *Rev. Argentina Dermatosisifilologia.* 1945 Dec. v 29 No. 4 257-62. [10 refs.]

Some nations, the Japanese for example believe leprosy to be incurable and therefore have no rules for discharge of patients. The author starts by stating the criteria of cure and calling for consideration of the following points: Absence of any clinical signs of activity; absence of lepra bacilli from the nasal mucosa, of active lesions of the skin, nerves or glands and absence of signs by biopsy; by biological tests and provocation tests (as the giving of potassium iodide) and Fernandez's test: the subcutaneous injection of lepromin.

The advantages of discharging patients are that the outlook of all is brightened, the morale of those remaining is raised by their realising the possibility of their own discharge inciting other patients to enter hospital in search of cure and reducing congestion of leper colonies. Its drawbacks are the need for keeping an eye on and exercising control over those liberated, watching for the first signs of relapse; indiscipline among the discharged; failure to attend for examination, changing residence and so on.

The author next gives figures quoted from the literature, to illustrate the frequency of relapsing cases and shows that the returns are very varied. HAYASHI gives the rate as high as 50 per cent., DENNEY as low as 3 per cent. CAMPOS gives 17.4 but the figure depends much on the type of disease—lepromatous cases 5 per cent. mixed 38 maculo-anaesthetic 12.6 per cent. and so on.

Definitive discharge he suggests, should not be absolute but should be subject to annual revision. The rest of this article is taken up with what is done elsewhere as at S. Paulo and the criteria mentioned in the foregoing abstracts.

H. Harold Scott.

- GARZÓN R. & ARGÜELLO PITT L. Conveniencia de unificar el criterio y la reglamentación de las altas en los enfermos de lepra. [Convenience of Unifying the Rules for Discharge of Lepers from Hospital.] *Rev Argentina Dermatosisifilologia* 1945 Dec. v 29 No 4 263-5

This covers much the same ground as the preceding abstracts. The authors stress the fact that everything depends on the type of disease, the frequency of examination the constant vigilance to discover the earliest signs of relapse be provisional discharge with constant observation and frequent re-examination before the final free release is granted.

H Harold Scott

- ARGÜELLO PITT L. & CONEJOS M. La bacteriología de la lepra tuberculoides [Bacteriology of Tuberculoid Leprosy] *Rev Argentina Dermatosisifilologia* 1945 Dec. v 29 No 4 909-11

In the Leprosy Congress at Cairo in 1938 the decision was reached that tuberculoid leprosy was not a fundamental form but merely a variety of the neural type. In the following year however at Brazil, the Congress decided that it was a fundamental form with characteristic histological changes. Epidemiologically it differed from the lepromatous in not containing bacilli and so was practically non-contagious. Others have maintained that the lesions may transitonally contain bacilli for days at a time perhaps for months.

To determine whether these lesions were bacilliferous or not the authors have examined 78 cases. BICHELLI in 1940 found 84 positive among 466 cases (18 per cent). FERNANDEZ in 1939 found 12 positive among 14 but all were in a reaction state. Among the authors 78 typically tuberculoid cases they found bacilli in 8 six were in a reaction state two were not.

H Harold Scott

- SPRECHER, A. Alterazioni patologiche delle ossa nella lebbra. [Bone Pathological Changes in Leprosy] *Pathologica* 1940 Apr. v 32 No 582 133-48 15 figs [24 refs] English summary

The author studies radiologically the pathological changes of the distal bones in twenty lepers with disease of various forms and in various evolution stages. He discusses the radiological findings obtained and reports a first brief histological pathological examination.

- OLMOS CASTRO N. & BONATTI A. A. Acerca de la propiedad floculante de los sueros leprosos [Flocculation of the Serum in Leprosy] *Rev Argentina Dermatosisifilologia* 1945 Dec. v 29 No 4 290-300 2 graphs. [25 refs]

This is a study of the precipitating property of the sera of lepers when in contact with a certain antigen and of the physico-chemical factors concerned, with a view to devising a method of sero-diagnosis of leprosy.

The antigen is obtained by boiling a leproma nodule in water for half an hour cutting it in small pieces bracing to a smooth paste in a mortar adding chloroform little by little evaporating this in a water-bath to obtain a residue of bacilli and lipoids. Sulphuric ether is added and the bacilli are separated by centrifuging. The supernatant fluid, rich in lipoids is evaporated in a porcelain capsule and the residue dissolved in 100 times its volume of 95 per cent alcohol. After being left for two days it contains a small residue and an amber-coloured supernatant fluid which is the antigen. About 0.05 gm. of

[September 1946]

lipoid or 5 ~ mlg. \* of antigen is obtained from 2 gm. of leprova tissue. Before use it is titrated as in the Kahn test and is suspended in 0.9 per cent. saline (usually 1 to 2.4 or 2.5).

Serum to be tested is inactivated at 56°C. for half an hour and for the reaction 0.3 cc. [mlg.] of the serum is placed in a well-slide and 0.05 cc. [mlg.] of antigen suspension is added. The two are mixed by rotary shaking for 4 minutes then covered with a Petri dish to protect from dust and evaporation, and the result is read off in 10 minutes. If it is positive there is a distinct flocculation, increasing during the next five minutes.

In 17 cases of the lepromatous type of disease the result was positive in 12, and in 3 out of 22 of the tuberculous type. Of 21 persons living with leprosy, but showing no clinical signs of disease, two had positive sera. None of 55 healthy persons reacted positively nor did any of 11 suffering from dermatoses of a non leprova nature. Trials were made varying the dilution of the serum, and in 3 out of 22 of the lepromatous type of disease the amount of antigen but the amount of serum, reducing or increasing the amount of antigen but the amount of all this was to show that the proportions used above were the best. The authors acknowledge that their results are not conclusive and the method cannot be regarded as satisfactory for the diagnosis of leprosy: they have merely essayed to study the reaction of the sera of leprova towards a specific antigen.

In the second part of this paper the authors report on tests of the sera of leprova by the Kahn, the Takata-Ara, and the Wolff reactions. They found that the results closely approximated those with the leprova antigen and concluded, therefore, that the leprova results are due to modifications in the colloidal state of the serum—colloidal instability due to physico-chemical changes in the serum.

BOVATTI, A. A. & OLIVERO CASTRO. \ Dosaje del complemento en sueros leprova. [Complement in the Sera of Leprova.] *Rev. Argentina Dermatofilologia* 1945 Dec. v 29 No 4 301-2.

This investigation was undertaken to determine the complement titre of leprova serum, on account of its possible importance as a factor of immunity in vivo and its value in precipitation reactions against a prepared antigen in vitro.

Thirty-five leprova sera and 64 sera from healthy persons were tested and the minimum quantity needed to produce total haemolysis in the usual haemolytic system in a mixture of various dilutions of serum made up to 1 cc. was determined. For the healthy persons the average was 0.03-1 cc. [mlg.] for tuberculous types of leprova 0.08 for lepromatous types 0.1 cc. [mlg.] Loss of titre is marked if the sera are not kept in the ice-chest (+5°C.). The authors conclude that the titres of complement in leprova sera are within the normal limits or slightly below them, and that the diminution is more marked in the lepromatous than in the tuberculous type. In no case was complement absent.

H. Harold Scott.

FERNÁNDEZ, J. M. M. & SOTO, C. M. Tratamiento de las complicaciones oculares agudas de la lepra con esteroles benzilicos del chaulmoogra por vía endovenosa [Treatment of the Acute Ocular Complications of Leprosy by Intravenous Administration of the Benzyl Esters of Chaulmoogra.] *Rev. Argentina Dermatofilologia* 1945 Dec. v 29 No. 4 268-72. English summary.

After a few introductory remarks on the seriousness of the acute ocular complications of leprosy and the unsatisfactory results hitherto obtained from the contraction mlg. is not explained. It cannot refer to milligrams since it is used throughout this paper as a measure of volume, e.g. for serum. Presumably it represents millilitres.—Ed.

treatment by intramuscular and subcutaneous injections of chaulmoogra (which often say the authors makes matters worse) and by protein shock milk calcium autohaemotherapy and other methods the authors give an account of their own investigations into the use of intravenous injections of benzylic esters of chaulmoogra (Neochaalmestrol)

The mode of administration was intravenously drop by drop starting with 0.5 cc. and repeating every 4-7 days and increasing the dose according to tolerance. The patients selected were lepromatous cases with ocular lesions which had proved refractory to the forms of treatment mentioned above. For small doses up to 3 cc. an ordinary hypodermic syringe was used injections being made slowly 1 cc. in 8-10 minutes. In most cases marked improvement followed weekly injections of 1.5-2 cc. In some cases a dosage as high as 10 and even 12 cc. at each session has been attained. The only untoward symptoms have been cough retrosternal oppression and dyspnoea.

The immediate results have been distinctly encouraging, for with the usual chaulmoogra treatment the eye symptoms may be aggravated and treatment consequently has to be stopped. With the new treatment the severe pain in the eyes associated with the ocular complications of leprosy disappears together with the photophobia, lachrymation and corneal oedema. Some of the good, it is thought may be due to pyretotherapy for the injections cause a rise of temperature to 38-39 C. with small doses to 40 and lasting longer with larger doses. The authors acknowledge that the method is only on trial but they put it forward in order that others may test it also.

Brief notes are given of 20 patients so treated the total dosage ranging up to 63.5 cc. and the duration of treatment up to 7 months. All improved some very early in the course and say the authors this drug seems to be the most efficacious of all those hitherto employed in the acute ocular complications of leprosy.

H Harold Scott

BLANCO J F Alcoholización del ganglio ciliar [Alcohol Injection of the Ciliary Ganglion (In Leprosy)] *Rev Argentina Dermatosisifilologia* 1945 Dec. v 29 No 4 275-7

Injection of alcohol into the ciliary or ophthalmic ganglion is recommended for relief of the ocular pains of leprosy. For preliminary anaesthesia the author injects at a depth of 4 cm. along the outer wall of the orbit and directed upwards 1 cc. of adrenovocaine (1 per cent novocaine with one drop of 1 per cent adrenaline) and follows this with 1 cc. of alcohol 60 degrees [presumably 60 per cent]. The consequent palpebral oedema, slight exophthalmos and subconjunctival ecchymosis subside in a few hours. In many lepers the ocular lesions—parenchymatous keratitis secondary to chronic irido-cyclitis atrophy of the iris synechiae pupillary occlusion repeated scleritis secondary glaucoma etc.—render the eye practically functionless.

Six cases are detailed all adults with advanced leprosy and severe eye symptoms as mentioned above and all within a few days were much relieved the pain photophobia and lachrymation disappeared. Moreover the effect was lasting the patients were seen periodically and six months after the injection the improvement was still maintained.

H Harold Scott

GUADAGNINI M Tratamiento de las úlceras leprosas por la novocaína endo-arterial [Intra-arterial Novocaine in the Treatment of Leprous Ulcers.] *Rev Argentina Dermatosisifilologia* 1945 Dec. v 29 No 4 278-82 2 figs.

The author is dealing with leprosy ulcers of neural origin in which the actual ulceration is preceded by bullae with serous or sero-purulent content superficial at first but later extending to the deeper tissues and in some cases producing the

typical perforating ulcer. They are commonest about the ankles and in the soles. The author's method of treatment from which he reports good results, is to inject 20 cc. of 2 per cent. novocaine into the femoral artery slowly taking 3-4 minutes over the injection. A feeling of heat is produced, which persists for 1-2 hours with rapid alleviation of the pain and ease of movement of the limb. The patient should rest for a few minutes to avoid the sensation of nausea from the novocaine. Injections may be given twice or thrice weekly.

H Harold Scott.

ARQUILLO PITT L. & ALBERTO CONSOLI C. Existe una susceptibilidad familiar en la lepra? Resultado de las observaciones hechas sobre 366 convivientes [Is there a Family Susceptibility to Leprosy?] *Rev Argentina Dermatosis filologia*. 1945 Dec., v 29 No 4 306-8

The authors' observations did not lead to a definite conclusion.

### HELMINTHIASIS.

RICCI, M. Elmintologia umana dell'Africa Orientale [Human Helminthiasis in East Africa.] *Riv di Biol Colon*. Rome. 1940 Aug v 3 No. 4 241-85, 20 figs. [Numerous refs.]

FLOCH, H. & DE LAJUDIE, P. Sur le parasitisme intestinal en Guyane française [Intestinal Parasites in French Guiana.] *Institut Pasteur de la Guyane et du Territoire de l'Inini*. Publication No 181. 1946 Jan. 4 pp.

BONCARDI, F. Reperto di *Physopsis africana* nel Sahara libico. [The Finding of *Physopsis africana* in the Libyan Desert.] *Riv di Biol Colon*. Rome. 1943 Jan.-Apr v 6, No. 1/2, 39-42, 5 figs.

TURANGUI M. A. Preliminary Notes on the Crustacean Vector of the Mammalian Lung Fluke (*Paragonimus*) in the Philippines. *J Parasitology* 1946 Apr., v 32, No. 2 150-51

Infestation by *Paragonimus* has been known in the Philippines for close on 40 years. MUSGRAVE having reported a case in 1907. It is however not widespread, but confined to certain localities. In 1941 snails (mostly *Velania*) crabs (*Potamon*) and prawns (*Palaeomon* sp.) were collected and examined. The first and last proved negative but of 216 crabs, 60 per cent. were found to be harbouring up to 50 cysts most in the leg muscles others in the gills, liver and thoracic muscles. Rats and cats fed on these developed adult *Paragonimus*. These crabs are eaten uncooked by the people, after removal of the legs, carapace and gills, or after shaking them with salt and keeping them for 24 hours. The metacercariae in the leg muscles were found to be still alive and infective for 7 hours after such treatment but not after 24 hours. If merely immersed in water they were still alive after 4 days. Sometimes the crabs are eaten uncooked after immersion in vinegar with a little salt in these circumstances the metacercariae were still alive 4 hours later and infective. The molluscan host has yet to be discovered.

H Harold Scott

SUBRAHMANYAM, R. Somatic Tasmiasis (Solium Cysticercosis) *Indian Med. Gaz* 1946, Feb. v 81 No. 2, 64-5 3 figs on 1 pl

COGGESHALL, L. T. Filariasis in the Serviceman. Retrospect and Prospect. *J Amer Med. Ass.* 1946 May 4 v 131 No. 1 8-12.

Many doctors in the United States will encounter filariasis for the first time on the demobilization of several thousand servicemen infected with *Wuchereria*

*bancrofti* during the war. The future of these men and the risk of secondary infection of others are matters of current importance. Bancroftian filariasis was common in the United States particularly some of the Southern States during the days of slave importation but when these ended the disease was unable to maintain itself and gradually diminished finally disappearing in 1925. A similar introduction and temporary lodgement occurred in Australia. At one time 10 per cent of all persons hospitalized in Brisbane suffered from the infection which eventually vanished spontaneously from the Dominion. After an account of the life cycle of *W. bancrofti* and of its epidemiology the author states that any doubts as to the susceptibility of Europeans to the infection which is rare among those in the Pacific under peace-time conditions were dispelled in 1942 on the entry of U.S. marines into the Samoan area. 38,300 men were exposed to risk of infection in areas of high filarial endemicity and 10,421 of them were considered to have become infected.

The diagnosis in the early cases was delayed owing to the lack of familiarity of medical officers with the disease but once its occurrence was recognized all cases of diagnosis were removed at once to the United States. The high infection rate in the marines in the Samoan area was not paralleled elsewhere with an equally high native incidence of the condition. The author explains this as being due to the greater segregation of the troops from the natives in these latter areas and to the differences in the habits of the vectors which in Samoa bite by day. The manifestations of the early disease (as recorded recently by numerous American workers) were quite unlike the text book descriptions of the later stages seen in natives reinfected over a period of years. Lymphangitis, lymphoedema and lymphadenopathy are the cardinal early signs and appear after exercise, subsiding with rest in 3 to 5 days. Details are given of the anatomical location of these signs which were sometimes associated with mild malaise, a slight leucocytosis and low-grade fever. Only 18 (0.07 per cent) of 2,590 patients seen over a period of 17 months had to be admitted to hospital for a flare-up of the disease. Fears of sexual sterility, impotence and elephantiasis were soon relieved in the psychologically sound and were proved by subsequent history to be quite unfounded. Diagnosis of the early infection is by no means easy and has to be inferred on clinical grounds. Examination of the skin reaction to a filarial antigen gave approximately 85 per cent of positive results in the infected but 15 per cent of normal persons gave false positive reactions.

The signs of early filariasis—happily in the absence of any specific treatment—vanish spontaneously if the patient is removed from the possibility of further infection. There is little reason to anticipate the re-establishment of the disease in the United States as an aftermath of the war in view of the light and transient infections being introduced there by the servicemen and of the fact that when introduced on a more lavish scale in the past in the highly infested slave population it failed to maintain itself and died out spontaneously. Release to civil life of the infected veterans can therefore proceed without danger to the community or to the individual. *A. R. D. Adams*

PLESSEN M. *Trichocephalus dispar* a Pathogenic Parasite. *Am Inst Med Trop* Lisbon. 1945 Dec v 2, 247-66 2 figs. [15 refs.]

DAY C. L. WOOD E. A. & LAKE, W. F. Observations on an Outbreak of Trichinosis among German Prisoners of War. *J Roy Army Med Corps* 1946, Feb v 86 No 2, 58-63

## DEFICIENCY DISEASES.

KING W D & SEBRELL, W H Alterations in the Cardiac Conduction Mechanism in Experimental Thiamine Deficiency *Pub Health Rep Wash.* 1946 Mar 22, v 61 No 12 410-14 3 figs (2 on 2 pls.) [33 refs.]

Various cardiac changes associated with thiamin deficiency have been reported. They include in man, shortening of the PQ conduction time, inversion of T waves increased QRS interval to bundle-branch block, sinus arrhythmia, sinus arrest premature beats auricular tachycardia, and tachycardia in rats bradycardia, shortened or lengthened PR interval, T wave and ST segment changes in pigeons heart block, tachycardia and inverted T waves in dogs deviations of the T wave, lengthening of the QT interval and tachycardia in swine bradycardia, prolonged PR interval, second-degree A V block abnormal P waves inverted T<sub>2</sub> nodal and ventricular premature beats, A V dissociation, complete heart block with ectopic ventricular rhythm, and auricular fibrillation. Many of these changes were associated with widespread necrosis in the myocardium.

Experiments with rats on a thiamin-deficient diet (except during periods of acute deficiency manifested by spasticity ataxia and convulsions at which time the animals were given 50 microgrammes of thiamin subcutaneously) showed that the average heart rate of the deficient animals decreased to 369 beats per minute progressively over a period of six weeks compared with a rate of 456 beats per minute for control animals and that in the deficient animals there was a progressive widening of the PR and QRS intervals as well as an increase in the amplitude of the QRS and T deviations. In 4 of 11 animals auricular fibrillation occurred during their first acute deficiency episode. In 3 of the 4 rats normal sinus rhythm was restored within 24 hours by the administration of thiamin, the fourth animal dying within 24 hours. In 4 of 11 animals during their second or third acute deficiency attacks, auriculo-ventricular nodal rhythm was observed one of the animals having previously shown auricular fibrillation. Premature beats, ectopic beats bigeminy auricular standstill and a shifting pacemaker were commonly found among the deficient animals. In two rats, auriculo-ventricular nodal rhythm was not converted to normal rhythm by large doses of thiamin and in one rat sectioning the vagi did not alter the auriculo-ventricular nodal rhythm.

The changes appear to be the result of abnormal tissue metabolism, and might be expected to vary in degree and persistence early or slight abnormalities being reversible and more severe deviations representing permanent damage to the tissues.

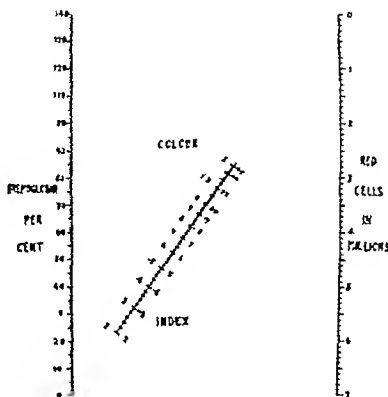
A clinical correlation between thiamin deficiency and thyrotoxicosis has been noted, and the similarity of the cardiac manifestations of thiamin deficiency and those of acute rheumatic fever in young adults has been commented upon. Consequently since auricular fibrillation may occur in experimental animals apparently as the result of chronic thiamin deficiency a possible factor in the cause of this arrhythmia in thyrotoxicosis rheumatic heart disease and the auricular fibrillation of unknown origin is suggested.

F Margatroyd

## HAEMATOLOGY

FREEDMAN B J Colour Index Nomogram. *Brit Med J* 1946 June 1  
838 1 diagram.

The colour index is read by placing a ruler on the appropriate points on the red cell and haemoglobin scales the point of intersection with the middle scale giving a direct reading



Colour index nomogram.

[Reproduced from the *British Medical Journal*]

To construct the nomogram draw two parallel vertical scales about 5 in. apart 1 in. on the scales representing 1 million erythrocytes and 20 per cent haemoglobin respectively the oblique scale is made by joining the two zeros and is calibrated by laying a ruler across the 5 million mark and the various haemoglobin percentages. It might be drawn on a card and varnished.

J F Corson

DARBY W J The Oral Manifestations of Iron Deficiency *J Amer Med Ass* 1946 Mar 30 v 130 No 13 830-35 3 figs. [Refs in footnotes.]

Six cases are described in which fissures at the angles of the mouth and superficial glossitis producing atrophy of the papillae accompanied chronic anaemia of iron deficiency type. Some of these cases were greatly improved or cured by iron therapy alone others responded to administration of iron after prolonged treatment with various preparations of the vitamin B complex.

The first of these patients a woman of 42 years had 10.5 gm. haemoglobin per 100 ml. She complained of rawness and burning of the tongue and lips



prunus vulvae listlessness and fatigue constipation and an attack of diarrhoea. Examination of the mouth showed fissures at the angles and a swollen dusky tongue with atrophy of the papillae. Treatment for 9 weeks with a mixture providing 12 mgm. thiamin 4 mgm. riboflavin and 100 mgm. nicotinic acid daily led to no improvement. She was then given 0.3 gm. ferrous sulphate thrice daily. Within a week there was marked subjective improvement. Within 3 weeks the tongue appeared normal the fissures were healed, and the prunus vulvae had gone. Iron therapy was discontinued after 5 months and the patient remained well during the succeeding 5 months.

The author believes that iron deficiency alone is a common cause of oral lesions that are confused with signs of deficiency of vitamin B. In his own clinic these signs are more commonly due to iron deficiency than to deficiency of nicotinic acid or riboflavin.

[It is unfortunate that the illustrations are so poorly reproduced as to be almost valueless.]

H. E. Harding

PINEY A. & HAMILTON PATERSON J. L. Sternal Puncture. A Method of Clinical and Cytological Investigation.

This book is reviewed on p. 870

## DERMATOLOGY AND FUNGUS DISEASES

ALLEN R. F. & GOODALE R. H. Pinta like Lesions among Natives of Guam. *U.S. Nav. Med. Bull.* 1946 May v. 48 No. 5 653-62 6 figs. [31 refs.]

In Guam particularly in the southern half of the island, a condition known as *peladang* is to be seen among the natives. It is characterized by hyperpigmentation of some and loss of pigment on other areas, on face hands and feet. The authors found 39 such cases among 2,006 natives inspected. 12 were males, 27 were females and their ages ranged between the wide limits of 21 and 83 years. Lesions started as small hyperpigmented areas with itching for a few days. These areas spread, and later the pigment was lost. There was no pain nor any systemic disturbance. Depigmented areas were greyish-white as a rule. In two patients they were of a pink colour. Biopsy sections showed atrophy of the epidermis and flattening of the *rete* layer. The dermis was infiltrated with lymphoid cells and oedematous, with chromatophores concentrated in the upper layers. The *stratum corneum* was thickened. Twenty-two out of 29 patients tested gave a positive Kahn reaction but only 56 were positive among 1,000 control natives. Dark field examinations were made of serum from six patients but no spirochaetes were seen.

Because much of the study of pinta has been carried out in Mexico, South America and the Caribbean islands, the disease has been thought of as almost entirely American, but it occurs also in Algeria, the Philippines, Malaya, Egypt, India, Ceylon, the Gold Coast and the Marshall Islands.

H. Harold Scott

BERLIN C. Degeneratio Colloidalis Solaris. *Harefuah* Jerusalem. 1946 May 15 v. 30 No. 10 [In Hebrew 240-41 2 figs. English summary 241.]

The colloid degeneration of the skin is a common disease in sunny countries. It affects fair-skinned individuals in advanced middle age with outdoor occupations. The eruption is strictly limited to the uncovered surfaces,

particularly the upper half of the face and the back of the hands. The morphological picture is variable. The familiar picture [is that] of small yellow closely aggravated [aggregated?] papules or pseudo-vesicles [but] one may find also smooth unelevated, shiny diffuse or island-like spots as well as rough and uneven structures closely resembling citrus peel.

The colloid degenerated skin is vulnerable brittle and tends to bleed. This condition was previously described by the author as *Purpura Solaris*. The nail phenomenon the appearance of a purpura streak after moderate to heavy pressure with the free border of the nail is pathognomonic of colloid degenerated skin and is of great diagnostic value in atypical forms.

Owing to the important role played by the sun in the production of this clinical entity the name *degeneratio colloidalis solaris* is suggested for it by the author.

MITRA S H. A Case of Madura Foot treated with Penicillin. *Indian Med Gaz* 1946 Feb 1, 81 No 2 82.

### HEAT STROKE AND ALLIED CONDITIONS

RENBOURN E T. Observations on Normal Body Temperatures in North India. With a Statistical Analysis by F F BONSALL. *Brit Med J* 1946 June 15 909-14 9 figs

The body temperatures of 894 soldiers—British and Indian—were recorded during the period from March to September 1945 at Dehra Dun North India. clinical thermometers were used and both oral and rectal temperatures were taken but not in every individual. Altogether 1,800 temperature recordings were made. The British soldiers had been in India for periods ranging from 4 months to 2 years. The figures of various records of groups of men are shown in tables and diagrams and are examined statistically and the original paper should be consulted for the details.

The following are some of the results and conclusions: oral temperatures up to 100.6°F and rectal temperatures up to 101°F may occur in normal individuals. the temperatures of British and Indian soldiers were much the same and acclimatization does not seem to be an important factor. resting oral temperature showed no correlation with erythrocyte sedimentation rate nor with the presence of prickly heat. temperatures rose slightly with the onset of the hot weather and fell at the end of the monsoon period. temperatures varied during 24 hours by from 1 to 2.6°F in 90 per cent of 38 diurnal curves of 14 individuals. exercise in the rain may cause a fall in oral temperature but in dry weather it causes a rise.

REES W H & OGDEN L W. Some Observations upon the Effect of Colour on the Absorption and Emission of Radiation by a Textile Fabric. *J Textile Inst* 1946 Apr 1, 37 No 4 T113-20 3 figs

This very concise paper deals with experimental tests which have yielded much needed information in regard to the relative effects of colour on the absorption reflection and emission of radiation falling within specified ranges of wavelength.

Samples of a standard poplin fabric dyed in a wide variety of colours were exposed to radiation from a high-intensity carbon arc emitting wavelengths closely corresponding to those in natural sunlight over a range of 0.2 to 1.5



in respect of the emission or absorption of long-wave radiation associated with such a temperature namely having the capacity for maximum emission maximum absorption and minimum reflection

It is noted that the properties of very low emissivity and low absorption possessed by aluminium foil are made use of in military topees and the design of tropical tents to make use of these properties is referred to

The concluding part of the paper draws attention to the fact that colours which appear roughly alike to the eye may have markedly different absorption characteristics particularly for the near infra red wavelengths which account for approximately 20 per cent of the total energy in sunlight at earth level. The inference is drawn that to ensure maximum protection against solar radiation dyes giving a minimum absorption in the near infra-red region should be selected. A plate showing infra-red photographs of the dyed cotton fabric is included in the paper and the problem of camouflage is referred to

G P Crouden

### MISCELLANEOUS DISEASES

SMITHBURN K. C Semliki Forest Virus. III. Propagation of the Virus in Developing Chick Embryos. *J Immunology* 1946 Apr v 52, No 4 309-14 1 fig

This paper records the successful propagation of the Semliki virus through 33 serial passages in the embryo chick (for a description of this virus see this *Bulletin* 1945 v 42 320). The series of passages was initiated with a filtrate prepared from an infected mouse brain injected into the region of the developing chick embryo [see ELIENBORG and SMITH this *Bulletin* 1937 v 34 692]. Eggs incubated for 7-9 days prior to inoculation were employed and passage was performed with a filtrate of ground-up embryo. Virus multiplied readily and embryos succumbed between the 11th and 24th hours after inoculation. Tests for the presence of virus were made by intracerebral inoculation in mice. The infective titre of embryonic chick tissue varied between  $1$  in  $3.65 \times 10^8$  and  $1$  in  $210 \times 10^8$  and there was no decline on passage. Detailed experiments showed that virus could be detected in the developing embryo from about the 4th hour of incubation onwards. The virus content seemed to remain more or less stationary after the death of the embryo. The curve of multiplication proceeded up to 12 hours by logarithmic progression. Beyond that point there was a flattening of the curve but a further absolute increase. Macroscopically the embryos showed varying degrees of hyperaemia and haemorrhage. Microscopic examination showed dilatation and congestion of vessels and extravasations especially in the subcutis. Necrosis of cells occurred only to a slight extent and was not marked in any special tissue.

A J Rhodes

WINKENWERDER W L Asthma—as observed Overseas in a General Hospital in the Southwest Pacific Area—with special reference to Relationship of Tropical Service to Onset and Recurrence. *Bull. Johns Hopkins Hosp* 1946 Feb v 78 No 2, 78-95

It is a curious fact that none of the standard works on tropical medicine deals with or even comments on, the ill effects of tropical climate and conditions on the asthmatic state or on the tendency for asthma to develop in such circumstances. This article has therefore a special value since it attempts to treat the subject scientifically.

The facts presented are based on a study and analysis of 209 cases among 352 American soldiers admitted to a South Western Pacific General Hospital during a period of two years ending July 1944 on account of asthma. These were readily divisible into two groups of nearly equal numbers—107 who had suffered from asthma prior to enlistment, and 102 who developed it after entering the service.

Among those in Group I a personal history of hay fever or asthma was elicited in 74 (69.1 per cent) and a family history in 59 (55.1 per cent) as compared with 48 (47 per cent.) and 30 (29 per cent) in Group II. The time elapsing between arrival in the tropics and recurrence or aggravation of the older-standing asthma was noted in 74 patients—in 62 (83.7 per cent) it was within 3 months and in 46 (62 per cent) within one month whereas among 61 who had no previous history of previous attacks 46 (75 per cent) developed symptoms in 3 months 3 within a week 14 within a fortnight and 27 within a month. The monthly distribution was examined in 104 of Group I and 61 of Group II. April and May accounted for 33 (31 per cent) of the former and most cases 16 of the latter occurred in May but the author on further study came to the conclusion that the date of arrival rather than environmental factors controls the monthly distribution of recurrence onset.

Several pollen extracts and inhalant dusts were tested for allergy of patients. Of 48 of Group I tested against the former 35 were positive, as compared with 22 of 25 in Group II. 74 out of 86 of Group I tested with inhalant dusts were positive and 46 out of 76 of Group II.

Attempts were made also to evaluate the immediate precipitating cause or combination of causes. Among those of Group I 2 were thought to be directly due to pollen alone 49 to pollen and inhalants 37 to inhalants alone, 5 to upper respiratory infection (sinus trouble polyp chronic tonsillitis) and 4 to lower respiratory infection, such as bronchitis or pneumonia. The respective figures in Group II were 0 15 12 and 20 to respiratory infections (no distinction is made between upper and lower) in 54 instances no determination could be reached.

Duration of disability differed in the two groups. In the first, the minimum and maximum days stay in hospital were 5 and 224 with an average of 80.24 in the second the respective figures were 6 161 and 57.7 days. Desensitization was undertaken in a few cases 28 to inhalant dusts 3 to pollen and inhalants combined and 7 to histamine. No valid conclusion as to the efficacy of these procedures was reached but in a small number of cases, such treatment appeared to be beneficial and abled the patient to remain on duty. [As stated, this is an important article although the number of patients was small. Abstraction has been difficult because many of the figures and calculations based on them are erroneously stated.]

H. Harold Scott.

MEARON I. G. K. Tropical Eosinophilia: some further Observations. *Indian Med. Gaz.* 1946 Feb v 81 No 2, 70-73 [10 refs.]

An interesting series of observations showing that the so-called tropical eosinophilia though most of the cases have been reported from India and Ceylon has in reality a wider distribution being found in China, Havana, America, Tanganyika, Samoa and other places. The author gives details of blood counts in patients with asthma, and useful diagnostic deductions therefrom. Thus, in one case with a total leucocyte count of 9,800 per cmm. ± 12 per cent. eosinophilia and an erythrocyte sedimentation rate of 2 and 5 mm. in one and two hours a diagnosis of asthma may be made with practical certainty. In another with a total of 10,000 an eosinophilia of 43 per cent and sedimentation rates of 10 and 30 W.R. negative and no response to

arsenic the diagnosis is in favour of asthma as against tropical eosinophilia. In a third with 13 000 leucocytes per cmm. 25 per cent eosinophiles without lung signs there was a personal and family history of asthma. But the patient was a child whose blood gave strongly positive Wassermann and Kahn reactions while in the parents they were negative and rapid improvement followed the giving of stovarsol. Hence the diagnosis is in doubt and the weight of evidence seems to be more on the side of tropical eosinophilia. Lastly an adolescent with a history of asthma with fever and cough a total white cell count of 49,500 an eosinophilia of 79 per cent sedimentation rates of 39 and 88 in one and two hours respectively, strong Wassermann and Kahn reactions and response to arsenic. Here the diagnosis would be tropical eosinophilia in a previously asthmatic subject. Intrapentoneal inoculation of blood of a tropical eosinophilia patient into guinea pigs yielded inconclusive results but only a single injection was given. The effects point equally well to infection or to reaction to a metabolic product derived from the organism or the patient's tissues. Further work is necessary in this but up to the time of writing the author had not been able to obtain fresh blood from a typical case of the disease.

JUNTER E. A. A Case of Tropical Eosinophilia (Weingarten's Syndrome) [Memoranda.] *Brit Med J* 1946 June 8 877 H Harold Scott

The patient was a European man aged 37 who had spent 12 years in Nigeria and during that period had suffered only from infective jaundice and subtertian malaria. Within 6 months of his return to England he began to have attacks of asthma at night with paroxysmal cough and orthopnoea the attacks were not very severe or prolonged. A skiagram of the chest was normal. A blood count made during an attack of malaria, showed 12 400 leucocytes with polymorphonuclears 20 per cent and eosinophils 59 per cent and there were some myelocytes. There were no signs of helminthic infection. No treatment was given and during the following year he had occasional attacks of asthma and another attack of malaria. About 18 months after the first attack of asthma he had a febrile attack lasting for some days with nocturnal asthma and widespread urticaria. His blood showed 36,200 leucocytes with polymorphonuclears 10 per cent and eosinophils 70 per cent. He was given three injections of neoarsphenamine (N.A.B.) at weekly intervals and improved rapidly when last examined his blood showed 5 800 leucocytes with polymorphonuclears 58 per cent. and eosinophils 5 per cent.

VAN DER SAR A Pulmonary Acanthosis. Its Relationship to the Eosinophil Lung and Löfller's Syndrome. *Amer Rev Tuberculosis* 1946 May 53 No 5 440-46 8 figs [14 refs] J F Corson

Writing from Curaçao the author gives a record of eight patients ranging in age from 8 to 48 years four of whom were sufferers from asthmatic attacks for short periods two of them for 3-5 weeks two for 3-4 months worse at night. The other four suffered from bronchitis but not asthma one had tuberculosis of the lungs. It is interesting that two of the patients were sisters living in a house where within the preceding 3 years two patients had suffered from tropical eosinophilia. In the sputum of each of the eight mites were found in one an adult *Tyroglyphus* in the others hypopal stages. They are well shown in photographs. X rays revealed enlarged hilar markings fine mottling and pulmonary infiltrations except in one case in which nothing abnormal was found. Blood examination showed leucocytosis ranging between 12 000 and 20 700 per cmm. with eosinophiles up to 80 per cent. at the beginning of

observations and final percentages between 4 and 11 after treatment four with malaricide injections [no dose stated] every 5 days, the others with carbazon [presumably carbazone] 3 times a day for 10 days [again no dose mentioned]. The total counts (after treatment) were normal (6,800 to 9,100) in seven reduced in one (4,500) the eosinophile percentage in two patients was reduced to 4 in two others to 5 and 7 respectively to 8 in three the one with 11 per cent had the lowest early total count 12,000 per cmm. [Many other observers have not found mites in the lungs and sputa of patients with tropical eosinophilia and the author seems to be begging the question in his conclusion. The question why in some cases the mite infection manifests itself as tropical eosinophilia in other cases as Löffler's syndrome and without any roentgenological abnormalities while a leucocytosis with eosinophilia persisted, must remain unanswered for the time being. It is still a moot point whether tropical eosinophilia and Löffler's syndrome are really different diseases.]

H. Harold Scott

WIKER, H. M. Roentgenologic Changes observed in Tropical Diseases. *Amer J Med Sci* 1946 May v 211 No 6 629-33. [11 refs.]

## GENERAL PROTOZOOLOGY

ADAMS F. H. HOKES R. & EKLUND C. Toxoplasmosis in Large Minnesota Family. *J Pediatrics* 1946 Feb. v 28 165 [Summary taken from *J Amer Med Ass* 1946 May 18 v 131 No 3 259]

Adams and his co-workers studied a typical case of toxoplasmosis in a 14-year-old girl who was a member of a large Minnesota family. The patient had 10 living siblings and 3 other close relatives. Complete physical studies including funduscopic examinations, were made on 11 members of the family. Neutralization tests against the toxoplasma organism were done on blood serum from these and four other members of the family group. Positive neutralization tests against the toxoplasma organism were present in the patient, her mother and 8 of 9 siblings tested. The mother and the 9 siblings had no clinical symptoms or signs of toxoplasmosis as determined by physical and roentgenologic examination. Whether infection in this patient and her siblings was congenital or acquired could not be ascertained.

HARNACK K. J. Trichomoniasis. A Twelve Year Study. *Western J Surgery Obstet & Gynecol* 1946 Feb v 54 No 2 61-4 2 figs.

The author who has been studying *Trichomonas vaginalis* infections for some 12 years gives in this paper his experience as regards diagnosis and treatment. For the former discovery of the organism by microscopic examination is essential though the occurrence of a secretion which "scalds" the external genitalia is very suggestive. For treatment the best results have been obtained by inserting Floraquin tablets twice daily for 12 days, followed by douching with a vinegar lotion two or more times a day for at least three months.

C. M. Wemyss

## GENERAL ENTOMOLOGY

HADDOW A. J. The Mosquitoes of Bwamba County, Uganda. IV. Studies on the Genus *Eretmapodites* Theobald. *Bull Entom Res* 1946 May v 37 Pt 1 57-82 9 figs [10 refs]

In 1941 after the isolation of the yellow fever virus from a human patient and from wild-caught mosquitoes in Bwamba intensive entomological investigations were started and are still proceeding. The topography and vegetation of the area has already been described and the results of day and night mosquito catches have been discussed [see this *Bulletin* 1946 v 43 79 80 255]

The present paper is chiefly of interest to the medical entomologist as it concerns the taxonomy and bionomics of eight species of mosquitoes of the genus *Eretmapodites* which occur in Bwamba. One of these is new to science (*E. ferox*) and is described. The larva and pupa of *E. inornatus* and the larva pupa and female of *E. penicillatus* are described for the first time. The author criticizes the diagnostic value of certain characters used in existing descriptions and keys and gives amended keys to the known males females pupae and larvae though some species still have to be grouped together.

Eggs of *Eretmapodites* are laid in small numbers at frequent intervals at the edge of small collections of water in such things as fallen leaves plant axils and snail shells. The eggs sink and are unable to withstand desiccation. Many experiments show that larvae of the Bwamba species prey on other small aquatic animals including mosquito larvae. Pupae move sluggishly and sometimes lie on one side as if dead. The genus is confined to forest and dense vegetation and females bite by day particularly in the late afternoon 6,500 In 1928 Bauer successfully transmitted yellow fever to rhesus monkeys by the bite of *E. chrysogaster* a species which will breed in small cages. The yellow fever virus has not yet been isolated from specimens taken in Bwamba though three strains of a virus related to that of Rift Valley fever have been isolated. It is suggested that species of *Eretmapodites* may include transmitters of human and animal viruses.

H S Leeson

DA CRUZ FERREIRA F & DE MEIRA M. T. V. Espécies de *Phlebotomus* de Lisboa e arredores. II. Sobre a presença de *P. ariasi* em Lisboa. [*Species of Phlebotomus found in Lisbon and its Environs. II. On the Female P. ariasi* in Lisbon.] *An Inst Med Trop Lisbon*. 1945 Dec v 2 207-15 2 figs (1 on pl) [14 refs] English summary

The authors have studied the morphology and recorded measurements of six specimens of female *P. ariasi*. In a detailed table they give their own findings and for purposes of comparison those of RAYNAL and LE GAC (1933) PARROT (1936-40) and ZARIQUEY (1937). They give the measurements of the head thorax abdomen palps antennae the wings the three pairs of legs and the spermathecae.

In a separate section of this article they record their study of over 4,000 specimens of *Phlebotomus* captured in Portugal during 1944. By far the majority were *P. perniciosus* 96.7 per cent. *P. minutus* came next 2.7 per cent. *P. ariasi* 0.4 and *P. sergenti* 0.2 per cent. The last were most common in fowl runs the others in human dwellings. The relative proportions of the sexes were *P. perniciosus* twice as many females as males *P. minutus* in equal proportions *P. ariasi* three males to one female *P. sergenti* five males to one female.

H Harold Scott



COOLEY R. A. [Senior Entomologist] & KOHLs Glen M. [Assoc. Entomologist U.S. Pub. Health Service] *The Genus Ixodes in North America. Nat Inst. of Health Bull. No 184* Wash. 1945 iii+246 87 figs. [40 cents.]

This monograph contains an account of the principal characters of the genus *Ixodes* with separate keys to females males and nymphs. These preliminaries are succeeded by systematic descriptions of 41 species females males and nymphs are considered separately for each species the various points being illustrated in line drawings, and there is a section for each species on hosts and geographical distribution in the United States, with a map. At the end there is a note on doubtful species a table showing geographical distribution, a classified list of hosts, and a list of references.

The monograph is of the high standard usually maintained in this series of National Institution of Health Bulletins and will be an invaluable work of reference to those interested in the subject  
Charles Wilcocks

STELLA, E. Nuovi dati sugli Ixodidi dell'Africa Orientale Italiana. [New Data on the Ixodidae of Italian East Africa.] *Riv di Biol Colon.* Rome, 1940 Dec. v 3 No 6, 431-5

VERBITT H. H. J. A Revision of the Family Acaridae (Tyroglyphidae) Order Acari, based on Comparative Morphological Studies. Part I. Historical, Morphological, and General Taxonomic Studies. *Canadian J Res Sect. D Zool. Sci.* 1945 Dec. v 23 No 6 139-68 33 figs. [32 refs.]

WISSEUP C. B. BROTHERS W. C. & EIDZ, P. M. Airplane Spraying of Rice Fields with DDT to kill Mosquito Larvae. *J Econom. Entom.* 1945 Dec., v 38, No 6 686-8.

Rice fields in Stuttgart Arkansas are first flooded when the rice is young in June then allowed to dry for the control of insect pests and then again flooded, in intention continuously throughout July and August. In practice however there may often be a series of alternate floodings and dryings during these months, and ideal breeding conditions for mosquitoes of the genus *Psorophora* and for *Anopheles quadrimaculatus* are produced. DDT applied from aircraft in xylene water emulsion at the rate of 0.1 lb. or more per acre gave perfect initial control of breeding up to mid-July when the thickening vegetation made bigger doses necessary of the order of 0.5 lb. per acre.

Under circumstances of this type it is essential that large areas of crop should be treated simultaneously, and therefore most desirable that some larvicidal effect be produced in fields which, though dry at the time of spraying, are flooded soon after. Very efficient pre-flooding control of this type was secured against *Psorophora* with doses of 0.2 lb. per acre or over. Against *A. quadrimaculatus* doses of 0.1 and 0.2 lb. per acre gave doubtful or no pre-flooding control, and of the two trials with 0.5 lb. per acre one gave good and one doubtful control.

Doses under 0.5 lb. per acre had a residual effect for about two weeks, during which no larvae were seen though mature larvae were not seen for a considerably longer period. With doses of 0.5 lb. per acre the initial complete elimination was maintained for three to four weeks.

No damage to developing rice could be observed during the season and random counts of heads of rice from treated and control blocks showed no difference in the number of plump grains that had been produced.

G. Macdonald.

FENNAN R. G. Preliminary Tests with DDT against Insect Pests of Food-Crops in the Lesser Antilles. *Trop Agriculture* Trinidad. 1945 Dec., v 22, No 12 222-8

This paper which is mainly concerned with the agricultural uses of DDT includes a table showing the mortality amongst about 40 species of insects of agricultural importance after exposure to standard doses of DDT. The author considers that in view of its concomitant effect on beneficial insects the question of whether DDT should be used on any particular crop in any particular Colony can only be settled by considering each case separately in the light of existing local circumstances. In the case of the major food-crop pests in the Windward and Leeward Islands there is little objection to its use.

A spray of DDT emulsion at 300 mgm. per sq. ft. on and around manure heaps had an immediate effect in controlling flies but little residual effect owing to the normal disruption of the surface which exposed untreated portions to which flies could gain access without damage. As a method of fly control in dairies it was concluded that complete treatment of exposed manure heaps at frequent intervals should be combined with limited treatment of carefully selected surfaces in the dairy such as hanging fixtures, sides of windows and doors, sunlit areas on walls and floor in the food mixing room, the mixing trough and the surfaces of sacks of feed. *G Macdonald*

STAMMERS F. M. G. & WHITFIELD F. G. S. Toxicity of DDT to Man. [Correspondence] *Nature* 1946 May 18 688 [Summary appears also in *Bulletin of Hygiene*]

At the Royal Naval School of Tropical Hygiene in Colombo a team of 15 men (1 Tamil and 14 Sinhalese) was employed continuously for 5 to 7 months in preparing and spraying a kerosene solution of DDT (5 per cent). On an average 24 hours per week were actually spent in spraying. At the beginning protective clothing and gauze masks were issued but owing to the heat the men refused to wear these protective devices. Most of the spraying was done in confined spaces and the men were often exposed to splashes and drip from the ceilings as well as to leakages from the sprayers (which received rather hard treatment). After a day's operations a white frost of DDT crystals could be seen on exposed portions of skin while overalls were frequently saturated.

Despite this very considerable degree of exposure to DDT none of the men developed signs or symptoms of intoxication. Each man was questioned as to general fitness and received a clinical examination. Liver function was estimated by the oral hippuric acid synthesis test, and haemoglobin estimations, red and white-cell counts including differential white-cell counts were made. Examination of urine for abnormal constituents and stools for parasitic ova, worms and cysts were also carried out. Similar examinations were made on a control group of men. No evidence of ill-health due to DDT was detected.

*J. R. Burnie*

## LABORATORY PROCEDURES

SPENCER, G. J. A Cheap and Speedy Method of Cleaning Old Microscope Slides. *Science* 1946 Apr 12 456-7

Slides and coverslips of preparations mounted in canada balsam are easily and quickly cleaned by immersion in a 10 per cent. solution of NaOH kept near its boiling point. Some form of slide holder such as a spiral copper wire

which will keep the slides separate from each other is necessary, and the hot NaOH can conveniently be kept in a beaker standing on a tripod over a low Bunsen flame. The slides and coverslips are afterwards washed in hot water

J. F. CORSON

**MONROE A. F.** The Serum Albumin and Globulin Levels in Africans as compared with Europeans with a Note on Technique. *Ann Trop Med & Parasit* 1948 Apr v 40 No 1 29-33 2 figs.

The serum albumin and globulin levels in 30 healthy young Africans serving in the army in the Gold Coast were compared with those of 30 Europeans from the Army in the area, all of whom had been in the tropics for some time. Proteins were fractionated by the cold methanol technique of **PILLEMEX** and **HUTCHINSON** (*J Biol Chem* 1945 v 158 299). The results by this method agree with those found by electrophoresis: the albumin/globulin ratio is about two-thirds of that given by neutral salt fractionation. A technique is described for filtering off the precipitated globulin without allowing the temperature to rise above 2°C in spite of tropical conditions, and without special apparatus.

The results are summarized in the following table —

Mean levels	Albumin gm per cent	Globulin gm per cent	Total Protein gm per cent	Albumin/ Globulin gm. per cent.
Africans	3.45	3.76	7.21	0.83
Europeans	4.3	2.58	6.88	1.7
Significance of differences	—	+	Doubtful	+

Even lower albumin globulin ratios were found in other cases: e.g. in five pregnant women, 0.45-0.7; in five children with nutritional deficiency, 0.3-0.9; in one case of hepatic cirrhosis 0.1

J. C. Waterlow

**ADAMS Margaret A. & BALLOU Alice N.** A Comparison between the Values for Plasma or Serum Protein as obtained by the Specific Gravity and the Micro-Kjeldahl Methods. *J Lab & Clin Med* 1948 May v 31 No 5 507-13 2 figs. [12 refs.]

1. One hundred and twenty-eight cases are presented in which the serum protein concentration was determined by both the micro-Kjeldahl procedure and by the copper sulfate specific gravity method.

2. In fifty-five of the 128 cases, or 44 per cent, the differences between the total protein values by the two methods did not exceed 0.3 Gm. per 100 c.c. of serum. The percentage of cases showing such agreement was slightly lower when the albumin was below normal or the globulin above normal. When 0.2 Gm. per 100 c.c. is taken as the criterion for duplication, only 35 per cent of the cases showed such agreement.

3. No conclusions could be drawn as to the type of patient in whom the serum specific gravity is influenced by factors other than the protein content.

4. The correlation between the specific gravity of serum and its protein content was found to be too low to permit the use of specific gravity determinations for reliable estimation of serum total protein."

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

KEAN B. H. Causes of Death of Children on the Isthmus of Panama. *Amer J Dis Children* 1946 Apr v 71 No 4 351-6

Complete post mortem examinations were made on 2,132 children under 11 years of age who died in the Isthmus of Panama during the 39 years from 21 October 1904 to 7 November 1943 histological sections were examined in nearly all cases. The children included British West Indian Negroes Panamanian mestizos (mixed Indian Spanish and Negro) and United States Whites. The causes of death the primary cause being selected are given in a table in which total cases groups in three periods of the 39 years sex groups and groups of race or origin are shown. Half of these deaths were due to —

Tuberculosis 217 malaria, 92 bronchopneumonia, 160 lobar pneumonia, 59 diarrhoea and enteritis 180 bacillary dysentery 29 congenital debility (under 1 year) 271 premature birth 184

The author does not discuss the subject.

J F Corson

LOWE J Some Recent Advances in Tropical Medicine. *Indian Med Ga.* 1946 Feb v 81 No 2, 86-96

CONNECTICUT STATE DEPARTMENT OF HEALTH Nomenclature of Pathogenic and Parasitic Organisms [OSBORN S H M.D. C.P.H. Commissioner Hartford, Connecticut 66 pp 1945 [Summary appears also in *Bulletin of Hygiene*]

This booklet is intended as a companion and supplement to the Physicians Guidebook to Public Health Laboratories published by Connecticut State Department of Health [*Bulletin of Hygiene* 1946 v 21 151]. It contains lists of the scientific names of organisms arranged in eight sections and in alphabetical order of genera in each section with short notes on each species. The sections include bacteria, rickettsiae fungi, protozoa and worms. The nomenclature of the bacteria is with few exceptions that of Bergey's Manual of Determinative Bacteriology 5th Ed. although that manual was being revised the author decided not to delay the publication of this booklet until the appearance of the revised edition. In the case of the fungi, Dodge's "Medical Mycology" was taken as the authority in other sections authorities were more in agreement as to the nomenclature. There is an alphabetical index at the end of the book.

This booklet will be very useful to medical practitioners in connexion with laboratory reports and in other ways.

J F Corson

## BOOK REVIEWS.

NAPIER, L. Everard [Companion of the Order of the Indian Empire F.R.C.P., etc.] The Principles and Practice of Tropical Medicine. pp xvi+917 195 figs. & 24 pls (4 coloured) 1946 New York The Macmillan Company 60 Fifth Avenue. [\$11 00]

On any count this is a good book. It is full, accurate readable and orderly and it gives throughout the impression that its author writes from an exceptionally wide personal experience, and that he has an enquiring mind. Where a point is in doubt he gives the arguments on both sides but generally makes up his own mind, one way or the other and says so. His writing is none the worse for a substratum of scepticism and a style which is at times sufficiently emphatic.

Naper makes it clear that he has written for the student, the practitioner and the public health worker and that the work is rather a textbook than a book of reference—but this is too modest a claim. He has deliberately omitted smallpox, typhoid fever, tuberculosis and the systematic mycoses but has included tularaemia. The chapters on bejel and leprosy were written by Dr H. SENEKJIE and Dr John LOWE respectively and acknowledgment is made of the collaboration of Dr R. N. CHAUDHURI, Dr Sundara RAO and others. It is evident that the author has been at pains to secure expert advice on many subjects. In a footnote it is stated that the first part of the book was published in India in 1943 and that the completed work has now been published in the United States—it is now available in Britain. It has been possible to make a few additions to the first part but for various reasons these have had to be strictly limited. This probably explains why the outstanding work on mepacrine both for treatment and suppression of malaria, carried out in the later stages of the war is alluded to somewhat briefly and that the doses recommended in the body of the chapter on malaria, which derive mainly from an experience of partly immune persons, are not so high as those quoted later and found necessary for non-immune soldiers operating in malarious countries. Many short addenda, referring to recent work, are included in these earlier chapters, and in later editions will, no doubt, be fitted more closely into the text.

The first chapters deal with environment, and with climate and its effects, including heat stroke and allied conditions—these are full of good sense. Medical men will generally agree with the author in what he writes of exercise, diet, drinking etc.—but it is not easy to get these ideas into the minds of the non-medical white settlers in the tropics.

The chapter on malaria occupies about 70 pages. It is very full, and the clinical aspect is particularly well covered—perhaps rightly the vast subject of anti-larval measures of control receives only general treatment, readers being referred to the special literature on the subject. The spray killing of adult mosquitoes is described more fully but DDT needs more mention. Incidentally DDT is not a mosquito repellent as is suggested on p. 118. Writing of malaria control Naper remarks that 'The economic aspect will always be paramount in this imperfect world. One's first thoughts must be how much will it cost and will it pay?' The reviewer must dissent—it is his belief that a doctor's first business is to promote good health, that commercial considerations must give way to considerations of human welfare and that it is the duty of medical men to insist on this.

The chapter on kala azar is very good indeed. The author has had a vast experience of the disease (he has seen more than 10 000 cases) has done much original work and has been closely associated with the research conducted in India during the last quarter of a century. The result is a highly informative and authoritative chapter fully up to date. This however is not quite true of the chapter on trypanosomiasis. For instance a sentence on p. 201 suggests that man is less susceptible to infection with *Trypanosoma rhodesiense* than with *T. gambiense*—the remark that sleeping sickness may be transmitted during coitus might be deleted—no mention is made of transmission by *Glossina pallidipes*—control measures are not very fully discussed. Nevertheless the bulk of the chapter is good and accurate. The theory of drug resistance which appeals to the author—that it is a matter of selection of resistant strains of trypanosomes—also appeals to the reviewer.

The relapsing fevers, leptospirosis, the fevers of the typhus group, bartonellosis, yellow fever, dengue, plague, tularaemia, the undulant fevers, and melioidosis are all adequately described, and the account of cholera is on the same high level as that of kala azar—here again there is evidence of a very wide

personal experience of the disease. For infections with *Entamoeba histolytica* the author prefers to discuss amoebic dysentery as the primary manifestation and to treat the other lesions due to the same organism as complications or sequelae. amoebic hepatitis is given a separate chapter. The flat statements on pages 428 and 429 that chlorination of water does not kill cysts of *E. histolytica* need modification in view of the work of CHANG FAIR and their collaborators [this *Bulletin* 1942 v 39 313 1945 v 42 286 734] who have shown that the concentration of gaseous chlorine needed to destroy the cysts lies well within the range of practicable superchlorination. Sprue is well described and a separate section is devoted to hill diarrhoea which the author thinks is usually caused by mild infection with *Shigella flexneri* but occasionally by some climatic factor *per se*. Leprosy is described in an excellent chapter by Dr John Lowe whose long association with the disease is well known to readers of this *Bulletin*. It is enough to say that the account is full and clear and is in line with modern views. Yaws, pinta and bejel are considered together the account of the last having been written by Dr Harry Senekjic. the treponemal aetiology of pinta is accepted.

The chapter on tropical skin ulcerations is followed by sections on lymphogranuloma inguinale and granuloma venereum and by a chapter on some common skin diseases.

Helminthic infections occupy 160 pages as befits their importance. The section on filariasis due to *W. bancrofti* contains much the same information as the separate paper which was reviewed in this *Bulletin* 1944 v 41 1054. The worms are classified in several ways (and there are three tables which the student will find most useful) but the final classification adopted for purposes of description is according to the main sites of the pathological processes they engender—intestinal parasites, parasites of lymphatics, subcutaneous tissues and serous cavities, blood flukes, liver and lung flukes, and worms that produce the main pathogenesis in their larval stage. It seems that any classification has unsatisfactory features. The accounts are excellent especially of those infections which occur in India. The nutritional disorders of the tropics receive full treatment and there is an interesting note on infantile cirrhosis of the liver by Dr R. N. Chaudhuri. The anaemias are briefly described and there are short chapters on snakes and rabies.

The author's experience has been gained chiefly in India, where he led an active and enquiring life for many years in contact with all that was best of medical research between the two wars. The emphasis of the book is therefore inevitably on Indian conditions and reflects the very great amount of research that has in fact been done there. It is primarily a clinician's book but the pathological and parasitological aspects are also very strongly written. It is not so full in matters of public health control but that is not peculiar to this text book. There is a great need for a modern book on tropical public health measures. As was stated at the beginning of this review this is an excellent book which can be recommended without reservation. The author has a very individual style which is an added attraction, and there is no woolly writing.

Some of the half tone plates are not clear and the coloured plates could be greatly improved.

Charles Wilcocks

KRAUS Heriberto *Tratamientos Modernos de las Enfermedades Tropicales de Colombia. Guia para el Medico Practico* [Modern Treatment of Tropical Diseases in Colombia. A Guide for the Practising Physician.] 343 pp. 1945. Bogota.

This is a graduation thesis and in his foreword Professor Camargo says: Among us where scientific publications are so scarce the work of Heriberto

Kraus is meritorious. The title describes accurately the substance and aim of the work, which bears testimony to the zeal and application of the author and to his facility for abstracting and extracting but it contains no original contributions. It deals with most of the diseases met with in Colombia the causes transmission symptoms diagnosis and prognosis receive little more than a mere mention and the title does not warrant our expecting more but treatment is fully dealt with. Quotations and references abound in fact, the whole is a compilation, the authors quoted and the references to the literature being fully noted in each case. The author has made full use of the *Tropical Diseases Bulletin* of 229 foreign that is non-Colombian references no less than 155 are to this *Bulletin* and this is amply acknowledged in the author's introduction.

In the cases of malaria leprosy and yellow fever fuller descriptions of the clinical aspect are given in others the diagnosis section comprises merely a list. One example may be given. Under lymphogranuloma inguinale called here *Lymphogranuloma venereum* we are told that Brumpt proposes that the causal agent should be named *Miyagawanella lymphogranulomatosis* nov. sp. and that in diagnosis the disease must be differentiated from soft chancre suppurations of the legs (presumably adenitis secondary thereto) tuberculous inguinal adenitis filarial adenitis inguinal herma gonorrhoea syphilis inguinal granuloma carcinoma or tuberculosis of the rectum, amoebic or chronic bacillary dysentery. No details are given regarding the general or differential diagnosis between these.

A work such as this does not call for a minute review. Suffice it to say that the work of extraction has been carefully done and consequently the Guide is a good one for the medical practitioner in the tropics at the present time. If it is to retain its usefulness revision will have to be frequent as new drugs are brought forward or new methods found beneficial and old ones replaced. There is no mention of food poisoning of any kind—rather a notable omission—and fish poisoning is concerned only with those which poison by their spines.

We have tested most of the directions and many of the references and found that the former are up to date and the references correct. Professor Camargo calls the work a minute and happy compilation of treatment which indeed aptly describes the publication.

H. Harold Scott

PINEY A. [M.D. M.R.C.P. Physician, St Mary's Hospital for Women & Children, London etc.] & HAMILTON PATERSON J. L. [M.D. M.R.C.S., Pathologist Redhill County Hospital Edgware etc.] *Sternal Puncture. A Method of Clinical and Cytological Investigation.* With a Foreword by the Rt Hon. Lord HORDER, M.D. F.R.C.P. 3rd Edition. pp. xv+80 13 pls. (12 coloured) & 2 figs. 1946 London William Heinemann—Medical Books—Ltd. [15s.]

The procedure of sternal puncture as an aid in the diagnosis and study of abnormal conditions in the bone marrow is of recent origin but has proved so useful that it is now widely practised, and there is a considerable literature on the subject and on the applications of the technique.

The authors have attempted to supply medical practitioners with a concise handbook giving a short account of the main types of marrow derangement and their correlation with the blood picture in each case.

Chapter I gives a useful account of the normal myelogram which must form the background against which the changes found in the bone marrow in various pathological states must be considered and the account if over-concise is probably sufficient with regard to the scope of the whole work.

There follow eight chapters on various blood disorders with descriptions of the changes seen in the bone marrow a mass of material which cannot be dealt with in detail in a short review but on which a few general remarks are made below

The last chapter gives a description of the technique of sternal puncture with rather incongruously accounts of methods used for vital staining and dark ground illumination of the material obtained as well as an account of mitosis

The arrangement of the coloured plates opposite the letterpress they illustrate is good and the plates themselves are well reproduced with the possible exception of that illustrating the bone marrow in malaria, where the representation of gametocytes and schizonts would be of little help in their identification in an actual preparation

The treatment of the subject matter of the chapters on various pathological states of the bone marrow suffers from the limitations of the very *raison d'être* of such a book i.e. an attempt at condensation of material not easily condensed. As an extreme example of this Chapter III may be cited. The entire chapter the subject of which is Leukaemoid Reactions consists of 25 lines and two words. The vagueness of the statements in this chapter apart from its extreme brevity would defy attempts to extract useful information from it either by the student or the professional haematologist. Another drawback to the book probably due to the same cause is the omission of some conditions one would have expected to see included such as Cooley's anaemia or erythroblastic anaemia and among the protozoal diseases infections with *Trypanosoma cruzi*

Typographical errors are too numerous indicating hasty proof reading and there are other mistakes possibly due to the same cause. For instance on page 32 the use of the word chapters instead of sections is completely misleading. In the section on protozoal infections there are some misleading statements. It is stated for instance that liver puncture does not usually give very satisfactory material for examinations. This is the reverse of true for kala azar since the material obtained by sternal puncture may sometimes show very few parasites although these are numerous in the spleen or liver of the same patient

The index to the book can only be described as extremely incomplete and is of very little use for locating any particular subject dealt with in the text.

Apart from the defects pointed out above the book would appeal to the undergraduate student, who would find in it a review of the subject giving information which could only be obtained otherwise widely scattered in the literature on haematology but the specialist and the worker in the tropics would probably prefer to consult the originals from which it is condensed

H. E. Short

ROY D N [AID D T M Professor of Medical Entomology School of Tropical Medicine Calcutta] Entomology (Medical and Veterinary) pp vii+358 162 figs. & 11 pls. 1946 Calcutta. Saraswati Library C18 & 19 College Street Market [Rs 30]

This volume is finely produced and illustrated and its general scope and arrangement at first sight suggest that it is well suited for the use of the medical officer in the tropics. Professor Roy is of course, fully qualified to write on Indian entomology and his account of certain aspects of his subject is excellent unfortunately however this standard is not fully maintained when dealing with arthropods whose importance is most marked in countries other than India.

The book is published in India but since no statement to the contrary is made, it is presumably also intended for workers outside that country. The



sub-title of the book indicates that the scope of the work is intended to cover veterinary as well as medical entomology, and indeed, the author states in his preface that the book was written "with the object of providing medical and veterinary students also public health workers with a treatise containing up-to-date information on the life history and bionomics of disease-carrying insects." This is a wide field and although the author does not separate the subjects the reviewer proposes, for the sake of clarity, to consider the veterinary and medical approaches separately.

So far as the veterinary aspect is concerned the reviewer is of the opinion that the information provided is usually inadequate for a serious student and that it is seldom up-to-date. To quote examples amongst the Diptera the part played by mosquitoes in the transmission of equine encephalomyelitis and Rift Valley Fever is not referred to—no description is given of the important part played by *Culicoides* in the transmission of filariasis to domestic stock and it is stated that *O. gibsoni* and other species of *Onchocerca* are possibly transmitted by *Simulium* (Cleland, 1927) (p. 177). *Babronema muscae* is mentioned as a parasite of the house-fly (p. 185) but no mention is made of *H. megastoma* or of the fact that as a result of transmission by house-flies the adult forms of these helminths occur in equines. *Stomoxys* (p. 221) is referred to as a vector of surra, but no indication is given that it also transmits *H. microstoma* and *Setaria cervi* to domestic animals and *Hymenolepis cariosa* to domestic fowls. Calliphorine myiasis is of vast importance to students of veterinary medicine, but the subject is dismissed in a few lines, and no reference is made to causal factor or to control. The important genus *Hypoderma* (p. 218) is almost equally cursorily dealt with, and the short description contains many inaccuracies—thus. The larvae of *H. bovis* are large and of greenish brown colour whereas those of *H. lineatum* are smaller and brownish grey. The larval life of *H. lineatum* is also much shorter. The effect of the parasite *H. bovis* on cattle is very serious. The growth is inhibited and the production of milk is reduced. It is not known how the larvae find their way to the animal's back as the eggs are always laid on the lower parts." The account of the *Mallophaga* (p. 290) is inadequate and contains the somewhat misleading statement that the insects belonging to the order are generally parasites of birds and one genus *Trichodectes* is found on mammals. The statement (p. 300) that "The causative organism of Texas fever is *Babesia bovis* or *B. bigemina* (sic) and is transmitted by *B. annulatus* and *B. decoloratus* Koch" suggests the quite untenable view that *B. bovis* and *B. bigemina* are identical. Psoroptic mange is one of the most important subjects to be dealt with in veterinary entomology, but Dr Roy dismisses it in some ten lines and these contain several inaccuracies thus. Scabies or mange in cattle is a specific disease of the skin caused by *Psoroptes communis* var. *bovis*. In sheep *Otodectes* produce the same type of disease (p. 330).

As regards the value of the book from the medical aspect the situation is somewhat different. The *Culicidae* and the *Musculidae* and their relation to disease are adequately and clearly described, although there are many statements which require alteration or amendment. For instance when describing the method of immunization against yellow fever Dr Roy writes (p. 130). "The person to be immunised is given a suspension of mouse-fixed yellow fever virus followed immediately by immune yellow fever serum from a recovered case of yellow fever or from a previously immunised person." This is obviously out of date and should be re-written. On page 52 it is stated that "In addition to malaria it is possible that some anophelines are capable of conveying the larvae of *Wuchereria bancrofti*." Later reference is made to the transmission of filaria by anophelines in India but their importance in Africa is omitted. Such generalized inaccuracies followed by subsequent corrections are not

uncommon. Thus it is surprising to find (p 244) that canine and infantile leishmaniasis are included amongst the diseases transmitted by fleas although previously (p 164) it is correctly stated that both diseases are transmitted by *Phlebotomus*. Again (p 215) *Cordylobia anthropophaga* is referred to as laying her eggs on the ground where there is smell of animal or human perspiration followed by the statement that the life history is incompletely known. Yet on the next page reference is made to the paper by Blacklock and Thompson in which the life-cycle is completely described. Most unfortunately some gross inaccuracies remain uncorrected throughout the book. When describing the life-cycle of *Dermatobia hominis* Dr Roy writes as follows. The eggs are laid on leaves and branches of trees which become attached to the ventral surface of the abdomen of [the] mosquito which mechanically transfers the first stage larva contained in the egg to the skin of animals. Almost equally misleading is the statement that Its presence in man is indicated by a painless tumour on the skin. Similar types of inaccuracy are allowed to remain uncorrected when dealing with such an important vector of disease as *Trombicula* (pp 319-321) the description of which contains the following statements. Only two species are of medical importance as they transmit in their larval stages the virus of a typhus-like fever these are *Trombicula akamushi* (Japan) and *T. deliensis* (Sumatra Java and India). The larval *T. akamushi* Brumpt is decidedly more reddish in colour than the larval *T. deliensis* Walch. Any transmission experimental work with *T. deliensis* is not easy. The adult mites of both sexes can be obtained often in large numbers from the ears of field rats. There is evidence to suspect that other arthropods in addition to mites probably also act as vectors. However mites appear to be the most important transmitting agent known at the present time. On page 305 the only animal reservoir given for *Rickettsia orientalis* is the bandicoot. This statement is correctly copied from a short paragraph which appeared in the *Lancet* of January 31st 1942 but the error has frequently been corrected in more recent articles on the subject.

The reviewer has pointed out these shortcomings and discrepancies not with a view to destructive criticism but in order to show that the book in its present form does not fulfill its avowed object of providing up-to-date information on the life-history and bionomics of disease-carrying insects. If the book were confined to medical entomology and if those portions of it which deal with aspects of the subject outside India were brought to the same standard of excellence as is reached in the description of the Indian culicidae the work would fulfil a useful purpose.

As already stated the general production and illustrating are excellent but proof-reading has been insufficient and many typographical errors and mis-spellings remain uncorrected.

R M Gordon

TOUMANOFF C [Docteur ès Sciences (Sorbonne) Chef du Service d'Entomologie médicale aux Instituts Pasteur de l'Indochine] *Les Tiques (Ixodidae) de l'Indochine. Recherches faunistiques avec indications sur les Ixodidae des pays voisins. Notions générales sur la biologie et les moyens de combattre ces Acariens.* [The Ticks of Indo-China. Biology and Methods of Control.] pp II+220 94 pls [Bibliography] 1944 Saigon. Instituts Pasteur de l'Indochine.

In 1924 the Government of Cochinchina instituted the Laboratoire d'Entomologie et d'Hygiène the primary work of which was directed towards the study of the mosquito vectors of malaria and other diseases of man and animals. Since the opening of the laboratory the staff have already published two monographs on mosquitoes the first by BOREL in 1930 [this *Bulletin*

1931 v. 28 335] and the second by TOUMANOFF in 1936 [*ibid.* 1937 v. 34 517]. The activities of the laboratory have however also included the study of various other arthropods of medical and veterinary importance and, in addition to the present monograph on ticks studies on fleas in relation to plague and the rôle of tabanid and other flies in relation to surra are in process of completion.

Dr Toumanoff divides his work into five parts. The first is devoted to the technique employed for collecting, preserving and examining the material. These methods conform to the usual standards but the author refers to his lack of success when collecting ticks from herbage by drawing a flannel cloth over the area. For observing the morphology of the tick by direct illumination the author describes and figures a simple viewing board, which can be attached to the mechanical stage of the microscope and which is grooved in two directions in order to receive a circular glass disk, to the centre of which the tick is temporarily attached. The remainder of the first part of the monograph consists of a brief but admirably clear description of the external anatomy of the Ixodidae, the terms used for the various parts and the classification adopted. Dr Toumanoff has accepted the general classification of Neveu-Lemaire in what is referred to as his recent work (it was published in 1933) but for defining the characters in each group he has followed Aragão and, mainly for genera not referred to by Aragão, Brumpt.

The bulk of the work—some 118 pages out of a total of 200—is devoted to a systematic description of the ticks recorded from Indo-China of which the author describes 36 species in the family Ixodidae and two in the family Argasidae. Of the latter only *Argas reserpilionis*, a parasite of bats, has been found by the author although *A. persicus* is said to occur in the Far East. In the reviewer's opinion the value of a systematic description can be estimated only when in use as a key that is to say when it is studied in conjunction with the actual specimens being described. Nevertheless the description of each of these 41 species is not only concisely given but is also accompanied by admirably clear and well-printed plates and text figures so that there seems little doubt that when this text is applied, all who are concerned with the identification of the ticks will be indebted to Dr Toumanoff.

The third part of the monograph is concerned, first with the general biology of the ticks and later with more detailed references to certain important genera and species.

In his introduction the author truly states that the study of the ticks affecting man and animals should be based on similar lines to those which have afforded invaluable information concerning the relationship of various species of *Anopheles* to malaria—a point too often forgotten particularly in veterinary medicine where sometimes little distinction is drawn between "a vector" and an important vector. In the fourth part of his monograph Dr Toumanoff deals generally with the rôle of ticks as transmitters of disease including in his account certain diseases such as tick-borne relapsing fever which have not been recorded in Indo-China.

The fifth and final section is concerned with control. The subject is dealt with generally with particular emphasis on the control of *Boophilus annulatus* var. *australis* in Cochin China. This part of the work and the sub-section devoted to personal prophylaxis although sound and interesting contain nothing new. The monograph ends with a short review of the natural enemies of the tick and their utilization in control.

In his foreword the author refers to his monograph as "a modest contribution to the subject of medical entomology in Indo-China." All workers in medical and veterinary entomology will place a higher value on this work, and will consider it a valuable contribution to an important subject.

It is unfortunate that in a volume otherwise so well presented the stitching and outer covering should be of so poor a quality

R M Gordon

PAMPANA, Emilio *Epidemiologia della malaria. Studi di Medicina e Biologia* [The Epidemiology of Malaria.] 403 pp 92 figs & 2 folding pls 1944 Rome Editrice Nazionale [L480]

This comprehensive text book on the epidemiology of malaria presupposes in the reader a fundamental knowledge of the clinical manifestations pathology and parasitology of the disease. It contains clear and concise accounts of the endemic and epidemic phenomena that characterize malaria in all parts of the world and few if any important contributions to our knowledge of the epidemiology of the disease have escaped the author's attention. To bring together so much miscellaneous material and to build it up into a coherent very readable treatise is a difficult task that the author has accomplished with distinction. Each chapter has an adequate list of references to the literature. Subjects treated include characteristics of malaria infection and the cycle of its transmission distribution of malaria in space and time climatic telluric and socio-economic factors in the epidemiology of malaria various forms of endemic malaria epidemic endemic and hyperendemic malaria anophelism without malaria and regression of malaria and a wealth of information concerned with the carrying out of a malaria survey.

The book was produced in difficult conditions and *errata* are unduly numerous but these are but small blemishes to an otherwise admirable volume.

Norman White

DOELEMAN H. *De malaria-epidemie te Middelburg in de jaren 1940 tot en met 1945, benevens een onderzoek van parasietendragers.* [The Malaria Epidemic at Middelburg 1940-1945 and Parasite-Carriers] [Thesis for Doctorate of Medicine Univ of Leiden.] 138 pp 6 plans on double pls & 2 graphs [Bibliography] English summary 1946 Goes Oosterbaan & Le Cointre NV

The freshness of a published doctorate thesis with its reminder of how a subject has reached current maturity is often one of its main attractions. Dr Doeleman saw his first malaria patient in 1940 and as a student at Utrecht had never heard of malaria except as a tropical disease which was said to occur also in some places in Holland. Middelburg the seat of his investigations on Walcheren is the capital of the province of Zeeland and has earned fame or notoriety not only in the recent war but in days gone by. During the stay of the English ambassador Cuthbert Tonstal at the Spanish court in 1517 the Zeeland fevers were greatly dreaded and drew from him the comment that no one left the province without disablement. He thought that the Styx and the Acheron rivers of Hell, must be situated close to this coast. An epidemic in the English Expeditionary Force which landed on Walcheren in 1809 and which was based upon Middelburg reduced that force from 40 000 to 15 000 men. Drainage and agriculture in South Holland just as in Scotland 200 years ago banished epidemic malaria. Zeeland was freed from epidemic malaria by the beginning of this century. The Zeeland fevers however were not all malarial. Among them were included typhus, the typhoid fevers and the dysenteries. Intermittent fevers and bilious fevers were not differentially diagnosed in the days when thermometers were not used and there were no laboratory investigations. The malaria parasite was demonstrated by the apothecary Van der Harst in 1900 a year in which Berdenus van Berlekom Jr described an epidemic at Middelburg.

Dr Doeleman follows his excellent first chapter on the history of malaria in Zeeland with four more chapters which cover systematically the epidemic and its control—investigation of parasite carriers, the principles of the campaign and epidemiological notes. Much of the information on the nature of the intermittent fevers of Zeeland has been culled from articles by Honig and Swellengrebel (this *Bulletin* 1927 v. 24 344) and due recognition is accorded to the first report by Schouten of the Malaria Commission of the Department of Health in 1920. It is to van Thiel personally that Doeleman expresses his thanks for support and with his name are coupled those of other members of this Commission: Schuffner, Swellengrebel and de Buck. Hulshoff Pol is another of the authors to whose investigations Doeleman pays tribute. From the views promulgated by these authorities and from his own researches Doeleman argues especially that the "healthy" parasite-carrier is the important and dangerous factor in the carry-over of malaria from the preceding autumnal months to the relapses in April and May of the following year—that the disappearance of parasites on clinical examinations of those who have been given courses of quinine in autumn does not necessarily denote complete eradication—that fresh infection takes place beginning in July and August and reaching its height in the autumn months—that healthy carriers do not sacrifice their premonition, or asymptomatic equilibrium between parasite and host by treatment with quinine and so on. Some of these features may be referred to in more detail according to the successive chapters.

In chapter II on the Description of the Epidemic and its Control we have the record of the author's own investigations and activity from 1942 onwards. He concentrated upon Middelburg where malaria had shown signs of increase in 1940. It would seem that the author is not disposed to blame the bombardment of Middelburg in 1940 with ruin of the town and development of mosquito breeding places in the cellars as more than merely one factor in the epidemic intensification; nor yet is he prepared to maintain that the inundation of Walcheren and the evacuation (11.9.44) of the people from the island banished malaria for the time being. Most of the inhabitants of Middelburg did not leave the town. The subject of relapse receives special attention—a factor which according to Korteweg is the crux of what is otherwise benign tertian malaria. A reference is made to the zoophilism of mosquitoes and to the finding of 20 000 *Anopheles* in abandoned horse stables. This is also referred to elsewhere and animals other than the horse are implicated, namely even pigs, rabbits and poultry.

For control Doeleman—while he does not in any way deprecate the value of work done on the breeding places of mosquitoes and the outhouses of human habitations—prefers to concentrate upon therapeutic measures designed to rid not only the human malaria patient but also and especially the dangerous healthy parasite-carrier of his plasmodia, and upon the detection of relapse cases. All methods of detection must be vigorously employed, blood examination, spleen examination and the like. As measures of prevention he recommends the spraying of houses in which malaria cases had occurred, with Shelltox, now likely to be superseded by DDT—and the autumnal administration of quinine to the malaria patients of the previous year in doses of 1 gm. of sulphate of quinine twice weekly on two successive days from mid August to the end of October—that is for a period of 8 weeks. It is to be noted that only quinine was available at this time. He does not minimize however the fact that this is a counsel of perfection which takes no account of the ineffectiveness of spraying apparatus or the difficulty that confronts a practitioner in persuading a person who is "healthy" and uncomplaining, to take a long and regular course of quinine.

In chapter III the investigation of parasite carriers is specifically dealt with. These are not restricted to children as they seem to be in tropical lands (by which is probably meant hyperendemic regions) in Holland—where less malaria prevails—carriers are distributed among persons of varying age. If malaria is really to be prevented altogether there must be efficient treatment of every infected person not only the malaria patient but also the healthy parasite carrier. The question of development of immunity is raised in order to stress the concept of 'premunition' as defined by Sergent which, as a latent infection and an equilibrium toleration of parasite by the host is compared with the allergic conditions of symptomless latency in tuberculosis and syphilis. Disappearance of parasites from the peripheral blood is well known and has been described as a retreat only to the spleen or more correctly to the reticulo-endothelial system.

Chapter IV treats of the principles of campaigning against malaria. The importance of this section lies in its insistence on the difference between the ideal and the practical. Doeleman seems to consider that the length of the course of quinine had no demonstrable influence on relapses and that a week's course of 1 gm. of quinine each day was economical practicable and within the disciplinary power of the practitioner. In the second place a knowledge of the bionomics of the mosquito and the time of the infectiveness of the *Anopheles* would save much futile effort. Thus to mention one example only the Dutch investigators have shown how much of the malaria of Holland is due to *Anopheles maculipennis atroparvus* breeding in brackish water and how little if any is due to *messeeae* which breeds in fresh water. The spraying campaign requires 0.4 to 0.5 litres of Shelltox per house and the house remains for some 14 days repellent to incoming *Anopheles* after which spraying must be repeated.

In his last chapter are various notes referring to malaria statistics to the question whether malaria in Middelburg is endemic or epidemic, with the conclusion that it is endemic and that an epidemic is only an exacerbation to the influence of live-stock on the persistence of malaria to the prognosis of malaria in Walcheren, as reclamation of its inundation devastation proceeds and it includes a short note on the problematical danger of therapeutic malaria infection in the treatment of dementia paralytica.

A hope is expressed by the author that his observations in Middelburg may be helpful to others faced with similar problems throughout Holland and we think that perusal of this monograph would undoubtedly be of great service.

W F Harry

MAGOON, E. H. [M.S. in San Eng. D. Eng. etc.] *Drainage for Health in the Caribbean Area*. [Spanish translation by J. A. HERNANDEZ C.E.] 556 pp. 80 pls. [Reprinted from Boletín Oficial Salubridad y Asistencia Social 1945 Feb-Oct v. 48 Nos. 2-10]

The business of malaria control has reached a higher stage of development in the Americas than in many parts of the Old World and there have grown up several classes of skilled people engaged in it. There is the technical specialist to describe whom we only have the ugly word malarialogist who is responsible for the general direction of policy and the preparation of schemes. There is a large class of malaria engineers specially skilled and practised in those branches of civil engineering on which malaria control may depend. There is also a group akin to our Sanitary Inspector and under him a large class of skilled artisans normally engaged in anti-malarial works and having some special knowledge of the problems particular to them.

This book is intended for the instruction of all of these groups except the first but mainly for the malaria engineer and the sanitary inspector. It gives

In the second part of this work, similar analyses are given of the oils derived from *Hydnocarpus wightiana* and *H. anthelmintica* which have been grown in the Belgian Congo. They show high content of hydnocarpic acid, low proportions of chaulmoogric acid—the first contains 12 per cent. of goicic acid, but the second very little. Among the conclusions are that both *C. ucheritschii* and *L. dentata* should furnish esters and sodium salts, and that their fractions, especially the lower melting point hydnocarpic acid fraction, are well worthy of trial in the treatment of leprosy. This memoir is a valuable one which should be consulted by all interested in the chemical composition of chaulmoogra oils as a class in relation to their use in the treatment of leprosy.

L. Rogers

Pozzo Adolfo. Peste de Oriente. Oriental Plague.] Prologos de los Profesores Carlos Fonso GANDOLFO & Carlos E. PAZ SOLDÁN. 259 pp., 77 figs. Bibliography. 1945. Buenos Aires. Editorial Alfa." San Martin 693

This systematic book on plague in paper covers should become a standard not only for the plague worker but for the practitioner. It has special importance naturally for Spanish South America and Brazil, and has detailed reference to Argentina. All aspects of plague are dealt with, beginning with biblical history, and passing on to the history of its introduction into the New World. The date of arrival at Monte Video in 1699 of the Dutch cargo boat *El Zier* from India is one which is generally accepted as the beginning of plague in South America, and the whole historical subject is dealt with in the first 42 pages. Formal reference chapters on Bacteriology, Symptomatology and Pathological Anatomy follow and bring us to the important subject of Sylvatic Plague. An illuminating analysis is given of the spread of plague in its stages from the port to the towns and cities by the railway system, from railway stations to the country, and then further into the country, largely as sylvatic plague. The author objects to the term sylvatic as insufficiently descriptive, and would use the term rural as the antithesis to port or urban plague. As the argument on sylvatic plague develops, it seems evident that the main factor contributing to epidemic human plague is still the rat, although field and semi-domestic rodents do contribute in a reverse direction to initiate rat epizootics. This is a very important contention because it suggests that anti-plague measures against rodents must, for economic reasons if no other, concentrate upon the rat. Under present conditions it is hopeless and indeed impossible to deal effectively with the sylvatic rodent on a country-wide basis. Fortunately, the danger of direct human infection from this source is more or less accidental and is likely to be confined to children or individuals who would utilize the pelt of a dead or sick animal. Prevention of such happenings can be effective up to a point by propaganda and by warning of this danger. Rat proofing and rat annihilation are the preventive measures *par excellence* so far as rodents are concerned. In the Argentine certain of the field rodents, some of them semi-domestic, are singled out for special reference. These are the Culs (*Microtus australis australis*) and Graomys (*Graomys griseoflavus griseoflavus*). Good illustrations are given of these as well as of the plague rats *R. norvegicus*, *R. rattus rattus* and *R. rattus alexandrinus*. Many photographs of places and procedure illustrate the text. Line drawings of the differences between the fleas *Pulex nosopsyllus*, *Xenopsylla citrocephalus*, *Leptopsylla* and *Ropalopsyllus* based on head, thorax and abdominal characters should prove useful. Other line drawings are of the "blocked" flea and of the distinctive features of the various species of the genus *Xenopsylla*—*chiroptis brasiliensis* and *astia*. The extensive bibliography would make a good foundation for a card-index to literature and has the great merit of giving the titles

of the papers as well as details of the publication. The work can be heartily recommended as sound and serviceable and especially Seneca's aphorism with which the text concludes —

*Longum iter est per praecepta breve et efficax per exempla* H. F. Harvey

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE. PUBLICATION No 18 Washington D.C. 1942. 130 pp. numerous illustrations. A Symposium on Relapsing Fever in the Americas. [Edited by Forest Ray Moulton] [19s.]

The American Association for the Advancement of Science unlike its British counterpart embraces the applications of science in medicine and public health and in recent years has published a series of volumes on important public health problems based on symposia arranged by the Section on Medical Sciences. Relapsing Fever in the Americas is the eighth of these volumes and comprises a series of papers presented at a symposium held in December 1941 at the Dallas Texas meeting of the Association. The 23 contributors represent workers in very different branches of the subject and their papers are grouped together under seven headings — introduction distribution parasitology tick vectors epidemiology symptomatology and public health aspects.

The historical introduction includes interesting notes on the life of Obermeier whose discovery of the spirochaete of European relapsing fever in 1868 opened a new chapter in scientific medicine since in his day bacteria had not yet been specifically associated with human disease. His death took place when only 30 years old as the result of injecting himself with blood from a moribund cholera patient in the hope of elucidating the cause of the malady.

The present distribution of relapsing fever in Oklahoma California Texas and Panama respectively forms the subject of four contributions and although comparatively few cases are recorded conclusive evidence is brought forward in support of the view that the infection is widespread in the animal population especially burrowing rodents. The vexed question of taxonomy is dealt with by H. G. JOHNSTONE who adopts WENYON'S proposal that the generic name *Traponema* should be used for spirochaetes both of the blood and of tissue. With reference to the specific name all relapsing fever spirochaetes are considered to constitute one species *T. recurrentis*. It is suggested that each different type might be designated by its geographical locality and specific intermediate arthropod host e.g. *T. recurrentis* California *Ornithodoros hermsi* strain or the *O. turicata* strain of *T. recurrentis* Mexico.

The unity or plurality of species is discussed by Gordon E. DAVIS who gives results obtained with three local (U.S.A.) vectors and their respective spirochaetes and with exotic species of ticks supporting the view that host-specific relationship offers the most accurate approach to the subject. Useful technical details are summarized in the section on laboratory diagnosis and cultivation of the spirochaetes which is followed by a discussion of the very complex problem of the relapse phenomenon in this disease. It is suggested by SCHUBART that the variable number of relapses (1 to 12) in tick-borne relapsing fever may be best explained in terms of the large number of possible antigenic phases, the number of these involved in each attack and relapse and the continuing capacity of the spirochaetes to produce new antigenic variants.

The article on tick vectors and life-cycles by Gordon E. DAVIS summarizes information on 25 American species of *Ornithodoros* of which only 5 are proved vectors to man. In addition R. A. COOLEY summarizes the specific characters and distribution of all known species of the genus a total of 44. E. FRANCIS



of labour migration from Ruanda across the Belgian border. In addition the effect of war conditions on African labour was investigated and the whole subject was discussed with the Governments concerned."

In general the African is a farmer cultivating for the maintenance of his family a portion of the tribal land of his village but not owning the land. The work is shared by all the members of his household and he is largely independent of wages. His needs are few and simple and it is only when his crops fail through drought or other uncontrollable cause that he is compelled to go to work for wages. He can ordinarily leave his family for months confident that they will not starve and will be protected by tribal ties and obligations. With a special object usually to gain a certain amount of money he travels long distances—hundreds of miles—to work on sisal estates or plantations etc. Higher wages instead of attracting him to stay longer merely enable him to leave earlier with the sum of money aimed at.

The author deals with labour conditions in relation to this background such matters as the welfare of Africans employed on large estates or by Government Departments including accommodation for families provision of hospitals and schools and social amenities questions of compensation for injury and illness trade unions the provision of camps on travel routes precautions against the spread of disease and many other important questions are discussed.

The needs of war produced some new industries and expanded existing ones factories for textiles leather goods dried vegetables dried milk timber production etc. were successfully developed, and the production of rubber pyrethrum and sisal was increased.

Occupational training the relationship of clerical and technical education to each other domestic training for girls juvenile labour especially in towns are important questions dealt with in this report.

The author shows the need for the establishment of properly equipped and staffed Labour Departments in these colonies and suggests how they should be constituted. The Head should be a Labour Commissioner with a seat on Council under him there would be Deputy Commissioners a Medical Officer a Trade Union Officer and Labour Officers. The problems that will arise in the future make it necessary to appoint men with special knowledge of their branches.

Conscription of labour and the immigration from Ruanda Urundi are discussed.

The Report is a most interesting one and will be of great value to all who may be concerned in the development of East Africa and the welfare of its inhabitants.

J. F. Corson

HONIG Pieter [Ph.D. etc.] & VERDOORN Frans [Ph.D.] [Edited by] Sciences and Scientists in the Netherlands Indies. *Natuurwetenschappelijk Tijdschrift voor Nederl. Indië* 1945 Vol. 102. Special Suppl. 491 pp. 134 figs & 1 folding map. New York City: Board for the Netherlands Indies, Surinam and Curaçao.

This extensive symposium of articles on all branches of science was collected by the Board for the Netherlands Indies and provides a summary of great historical interest. For the medical reader the chapters on the history of cinchona the relation between soil and population density rabies research, medical contributions from the Netherlands Indies and medical education, will be of most interest. These chapters form a small proportion of the mass of information on many diverse subjects of scientific interest the contributors to this volume are eminent in the subjects with which they deal.

Charles Wilcocks.

# TROPICAL DISEASES BULLETIN.

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## COMPOSITION OF MOSQUITO LARVICIDES

By G MACDONALD M.D. D.P.H. D.T.M.

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A very large number of substances have been used as mosquito larvicides but only a few are or are likely to be in general use. They may be classified according to whether they are applied as surface films as floating powders, or in suspension or solution. Only those in the first category are generally useful under all circumstances though Paris green in the second has had big advantages in special conditions. With the introduction of DDT surface film larvicides are likely again to be the most widely used—a preliminary understanding of the properties of films is essential to their proper selection and use.

### *Oil Films*

An oil film whether used as a direct larvicide or as a vehicle for another such as DDT must have certain qualities of spreading power and stability and if used alone it must also be toxic to larvae. The spreading pressure expressed in dynes per cm. is a measure of the force exerted by a film to overcome resistance to its spread. In the case for instance of highly purified medicinal paraffin it is 0 dynes/cm. and the paraffin will not spread even on an entirely clean surface. Kerosene usually has a value of about 10 dynes/cm. gas oils of 13 to 16 dynes/cm. and they will spread on many moderately clean surfaces but are often prevented from doing so by naturally occurring surface contaminations. A good larvicidal oil for general purposes should have a spreading pressure of not less than 23 dynes/cm. and if self-spreading sufficient to penetrate deeply amongst vegetation and against most naturally occurring obstacles is needed oils with very high spreading pressures of the order of 46 dynes/cm. should be used.

ADAM (1945) has described a simple field method for the estimation of spreading pressure by opposing successive members of a series of oils with known spreading pressures against the unknown oil on a clean water surface by which means it is possible to find the place of the unknown in the known series. The test needs few and simple materials and apparatus: terpeneol technical quality, oleyl alcohol, pure medicinal paraffin, an 8-inch glass funnel retort stands and running water and can be carried out in a very primitive laboratory. The main details are excerpted in this *Bulletin* 1946 v 43 255.

The spreading pressure of natural oils is largely dependent on the presence of impurities exerting surface action and it can be reinforced by the addition of spread-aids. Vegetable oils and fatty acids such as crude castor oil

(1-2 per cent) and oleic acid (0.5 per cent) are commonly used for this purpose but have the disadvantage that they decrease the stability of the films. Ceryllic acid is without this disadvantage and may usefully be added in proportions of 0.25 to 1.5 per cent. Commercial resin is a good spread-aid; a concentration of 0.25 per cent greatly raising the spreading pressure, though it has the disadvantage that it is difficult to dissolve. In the process of refining oil the spread-aiding substances tend to be concentrated in some of the by-products which are then used to increase the spreading pressure of special larvicidal oils which, on the whole, are of good quality. In no case should substances soluble in water such as phenols or saponated cresol, be used, as the action is quickly reversed and soon results in a decreased spread.

MURRAY (1938) has shown that the stability of films is in part due to the qualities of the hydrocarbons constituting the oil and in part due to dissolved polar substances some of which increase and some of which decrease the permanence of the film. To secure maximum stability the oil should consist of a mixture of wide and overlapping cuts with either very high or very low aromatic content and should not contain fats or fatty acids as spread-aiders. This quality can best be judged by an empirical field test applying the oil under natural conditions on a windless day and rejecting any specimen which does not form a stable film lasting at least two hours.

Oils appear to vary very much in their toxicity to larvae but in reality they vary more in rapidity than in certainty of action. MURRAY (1936) has shown that once oil enters the tracheal system, the ultimate death of the larva is almost inevitable but may occur in a few minutes or be delayed until pupation is due. The best penetration is secured with oils of medium (200-300°C) boiling range and highly volatile substances may have an irritating effect which causes the larva to avoid contact and so to escape destruction. In testing oils for this quality a film 10 microns thick (1 cc to 1 000 sq. cm) should be spread on the surface of water in which there are about 50 larvae. After 30 minutes the larvae should be removed without being artificially contaminated preferably after the water surface has been cleansed by allowing the receptacle to overflow and the death rate should be recorded at the end of one hour from the beginning of the test in which time a good oil should kill all larvae.

When oil alone is used as a larvicide the object is to spread a film not less than 10 microns thick, which corresponds to 14 gallons per acre or 0.3 gallons per 1,000 sq. ft. though in practice larger quantities up to 25 gallons per acre are commonly used. With the type of oil normally used with a spreading pressure of about 23 dynes/cm. a film can be expected to form, but deep penetration against natural films cannot be relied on. The oil must be sprayed over the entire water surface where larvae may occur. Substitutes such as drip-cans and oil-balls may work under some circumstances, but are very unreliable.

#### *DDT Solutions.*

DDT applied in solution as a surface film, has a minimum practical lethal dose of the order of 10 mgm. per sq. metre i.e. 1.43 oz. (or 1.43 pints of 5 per cent solution) per acre though the dose applied is usually greater than this of the order of 4 pints per acre. Larvae are killed fairly rapidly and first instar larvae re-appear in a few days but the number of larvae (particularly of fully grown ones) remains subnormal for a period which may be as long as a month. Apart from this rather unreliable effect there is no residual action comparable with that exerted when DDT is applied as an adult insecticide and it seems that the DDT is removed from the water through a physical effect of the bottom mud complex and of suspended material (ARNOLD

FERGUSON and UPHOLT 1945) Conversely UPHOLT GAINES SIMMONS and ARNOLD (1945) have shown that a very prolonged residual effect is exerted in water free from mud such as the containers commonly accepted as breeding places by *Aedes aegypti* and that its use on this type of water may revolutionize *Aedes* control

Several workers have shown that effective spread of DDT solutions occurs from the point of application and RIBBANDS (1945) has recommended the abandonment of the usual spraying technique and the substitution of discrete applications from an oil can or similar means. In his trials doses of 4 cc. of 5 per cent solution produced a complete kill for a minimum distance of 25 ft. along the bank from the place of application and in one case for 70 ft. despite the presence of moderate vegetation. He found that oils commonly used were quite effective for this purpose but the reviewer has had failures of spread on still waters in Iran and advocates the use of specially prepared oils with really high spreading pressures over 46 dynes/cm. for this purpose. In one of his trials of a 5 per cent solution of DDT in a specially prepared oil eight discrete applications of 65 cc. destroyed all larvae in 4 000 linear feet of stagnant irrigation channels containing moderate vegetation the total area treated being 16,250 sq ft and the overall dose 2.5 pints per acre. Solutions in other oils applied to very similar waters failed to penetrate natural obstacles and left many living larvae.

If the full advantage of DDT is to be utilized, this method of discrete application must replace spraying. Much experience with it is to be gained before the technique can be accurately laid down but as a working basis for extensive trial it is suggested that a 5 per cent solution of DDT in a stable oil with a spreading pressure of not less than 46 dynes/cm. should be used, and that on still water it should be applied in individual doses of about 2 oz. which should be sufficient to destroy larvae over an area of about 2 000 sq ft (the area of a circle of radius 25 ft.) from the point of application.

During the war there has been a very rapid development in the distribution of DDT solutions from aircraft. The strength of solution the solvent and the dose are much the same as in the case of ground application. Various types of apparatus have been used in the simplest the stream of solution leaving a controlled outlet is shattered into a mist by the violence of the air current it meets on emergence. In others the solution is discharged into the exhaust and a fine aerosol is thereby produced. Designs of apparatus have been developed in the normal secrecy of war and the reviewer does not know of a published description of the type he considers suitable. With most techniques the lethal swathe is about 200 ft. broad. As one ton of solution is sufficient for 450 acres or for a 200-ft. swathe some 18 miles long very large areas can be quickly and effectively treated with the additional advantage that such of the solution as falls on vegetation serves as a residual insecticide to destroy ovipositing adults. There is immediately a great reduction in mosquito density—a point emphasized in the work of LINDQUIST and McDUFFIE (1945). The cost of maintenance of aircraft of the types commonly used in the war is so high that the techniques cannot be widely used in peace time though apparatus for smaller aircraft may be developed for the treatment of large water areas.

#### *Floating Powders*

Floating powders as larvicides were first advocated to take advantage of the special feeding habits of anopheline larvae which skim minute particles from the surface. For this reason the powders are destructive to anophelines only and are generally useless in moving water from which they may disappear before being ingested. Paris green has become recognized as the most

generally suitable of such larvicides though many others such as copper cyanide copper arsenite and calcium arsenite have been quite extensively used. Pure paris green contains 56.6 per cent. of arsenic as  $As_2O_3$ , and commercial samples should contain nearly this amount preferably over 53 per cent and certainly never less than 50 per cent. The particle size is important as only the smaller particles are ingested. METCALF and HESS (1944) showed that the average maximum sizes of particles ingested by *Anopheles quadrimaculatus* larvae were 29 51 68 and 106 microns for 1st 2nd 3rd and 4th instar larvae. It is usual to specify that all the paris green should pass through a 200-mesh bolting cloth and that it should leave very little residue on a 300-mesh bolting cloth. Paris green answering such a specification contains many particles of excessive size and most of the particles may be too large for ingestion by 1st stage larvae. Better results may be secured with very finely powdered preparations in which most of the particles are about 2 microns in diameter. For aircraft distribution, however very finely divided paris green is too liable to be drifted away by gentle breezes and a slightly coarser material is required. Metcalf and Hess recommended a quality in which 84 per cent. of the particles were between 20 and 50 microns in diameter. As there may be other unappreciated factors which affect its utility, it is usual to specify that samples should be submitted for laboratory trials to verify their lethal effect.

It is very difficult to assess the minimum lethal dose of paris green owing to the difficulty of ensuring complete and even distribution of minute quantities. With a product of good quality carefully and evenly distributed by a skilled worker a complete kill can be obtained with doses of about 4 oz. per acre but this is so wasteful of time that in practice a dose of 1 lb. per acre, which allows for some irregularity of distribution is now commonly accepted.

The whole trend of practice has been to emphasize the importance of simplicity of technique and the advantages of hand distribution over the use of mechanical sprayers in the treatment of all water except extensive swamps and even in the latter case the simpler technique should be used unless the labour is highly skilled. For hand distribution the strength of the mixture should be 1 per cent. and any dry dust or powder may be used as a diluent the mixture being made in a bucket with the aid of two measures to hold 1 or of paris green and 99 oz. of dust respectively and a wooden stick as a mixer. The mixture is then scattered by hand one normal handful being adequate to treat a circle of 4 ft. radius.

Where the extent of the water to be treated makes the use of mechanical "dust guns" inevitable a 5 per cent. dilution of paris green in some extremely fine powder preferably powdered soapstone or soft stone should be used, the mixture being made if possible in a cement mixer at some central site and distributed ready mixed to the place of application. It has been common to use a 33 per cent. mixture for aircraft distribution but when this is indicated, DDT has such manifest advantages that the use of paris green will probably now come to an end.

#### *Emulsions and Suspensions*

A number of substances have been used in emulsion form as larvicides phenol in the original Panama larvicide creosol, pyrethrum and now DDT. None of them has permanently established itself for general use and probably none will. In the case of DDT the tendency has been to make a 5 per cent. solution in fuel oil and to emulsify this with an emulsifying-spreading agent (unfortunately always described under a proprietary title) in about 30 times its volume of water thereby producing a larvicide to be used in doses comparable with the dose of oil—15 to 25 gallons per acre. The method may

save some of the material cost of oil it saves none of the labour which is the chief cost of oil distribution and self spreading such as described for DDT surface films cannot be relied on. The method may be of special use in the treatment of minute breeding places such as those of *Aedes* where applications of oil solutions of DDT might be very wasteful in which case the dose is arranged to secure a final dilution of about one part DDT per million parts of water.

When liquid based paris green was introduced by BARBER RICE and MANDEKOS (1936) it was carried in the oil phase of a kerosene water emulsion and was particularly suitable for the treatment of small breeding places including those in which the water was running. AZIZ (1939) later developed the use of plain suspensions of paris green in water and until the introduction of DDT this remained the most effective method for the treatment of shallow moving water in places where transport difficulties made the carriage of oil impossible or unduly expensive. The paris green which should be of normal grade and not the extremely fine grade referred to above is mixed with water in the spraying machine from which it is to be applied, in sufficient quantity to give a 1 in 500 or 1 in 250 suspension which is kept evenly mixed by occasional agitation of the machine. It is sprayed on the breeding place in sufficient quantity to give a minimum of 1 part or preferably 1.5 parts of paris green per million of water that is for a 1/500 suspension sprayed on water 3 inches deep one gallon to 870 sq ft. It has proved itself of exceptional value in the treatment of the shingly streams commonly used as breeding places by *Anopheles superpictus* in the Mediterranean area though recent experience suggests that DDT solutions may largely replace it.

Each of the larvicides described has some special qualities which make it more or less suitable for use for different kinds of breeding places or in different circumstances and each of them will probably remain in wide use. In any one scheme of mosquito control it is desirable to use the minimum possible number of methods and preferably one method only. To this end the method which is most generally suitable for the common conditions locally encountered should be chosen and adapted to as many of the local conditions as possible even though it may not theoretically be the most desirable for all of them. Only by this selection of methods can the proper training of subordinate labour on whom success finally depends be secured and the occasional use of a method which may not locally be the most economical is preferable to the confusion which arises when a choice of methods is left to men unqualified to make it.

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## SUMMARY OF RECENT ABSTRACTS.\*

## VIII TYPHUS GROUP OF FEVERS.

*General.*

GEAR (p. 362) gives an account of the rickettsial diseases of South Africa. Louse- flea and tick typhus are widespread, and the last can usually be distinguished from the other two clinically and by the Weil Felix reaction.

WOLSTENHOLME and GEAR (p. 877) discuss the various serological tests used in the differentiation of fevers of the typhus group. Most reliance is placed, for various reasons on the complement fixation reaction but as pointed out by MEGAW in comment this test does not always distinguish epidemic from murine typhus though it is usually effective in the diagnosis of the tick-borne group. See also PLOTZ *et al.* below.]

BENGTSON (p. 983) sums up the experience of the complement fixation test in the rickettsial diseases. She thinks it highly specific it can be used in retrospective diagnosis and in rats, and may become a routine procedure complementary to the Weil Felix reaction.

FITZPATRICK (p. 982) reports a study of the rickettsia agglutination test in the diagnosis and differential diagnosis of epidemic and murine typhus and Rocky Mountain spotted fever. The test is capable of distinguishing between epidemic and murine typhus usually by a difference in titre of the reaction to the two antigens differentiation of these from Rocky Mountain fever is more clear-cut. Details should be sought in the original abstract.

BLANC and BALTAZARD (p. 714) have carried out extensive research into the question of immunity in fevers of the typhus group. A frank attack of epidemic or of murine typhus immunizes against both infections for at least several years. Rocky Mountain spotted fever and boutonneuse fever also immunize against each other. Inapparent infection produces immunity and inapparent reinfection must be very rare. Hereditary transmission of infection in ticks readily explains persistence of the tick borne fevers but this does not occur in lice or fleas. The same authors (p. 715) state that of the two groups of typhus fevers louse-borne and flea borne on the one hand, and tick borne on the other neither can be transmitted by the vectors of the other. Murine rickettsiae can however be transmitted by lice from man to man. They do not think that inapparent attacks are important in maintaining louse-borne typhus during inter-epidemic periods but think that infection from dried, infected louse faeces is the cause of sporadic attacks and may initiate epidemics. Infected louse faeces are quickly inactivated by moisture and sterilization of clothing by steam is reliable. Louse control, by itself, is inadequate as a means of checking epidemics.

EYER and RUSSA (p. 23) have studied the morphology of rickettsiae by means of the electron microscope.

DARZINS (p. 544) describes a method of staining rickettsiae details of which should be sought in the original abstract.

*Vaccination.*

SCHULTEN (p. 27) quotes figures which indicate that typhus in previously vaccinated persons is milder and of shorter duration than in unvaccinated controls. BILBIN (p. 796) notes that in persons vaccinated against typhus the onset of the disease when it occurs is rapid, but its course is usually mild. Diagnosis may be difficult.

The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

DURAND *et al* (p 107) tested the sera of a group of people in North Africa before and after inoculation of various vaccines by means of a protection test in which infective material was mixed with the serum and then injected into the skin of rabbits. Some of the sera gave protection before vaccination but many more after vaccination. Killed vaccines appeared to be more effective than live.

From experience of vaccinating mice FITZPATRICK (p 793) concludes that the toxic factor in epidemic and murine strains of rickettsiae is identical.

LEVKOVICH and PETRISHCHEVA (p 268) find no difference in effectiveness between vaccine of the Cox type mouse lung vaccine and vaccine prepared from lice except that one prepared from the whole bodies of lice may cause allergic skin reactions. They give details of their methods of dealing with the lice.

DOBOVICK and WYCKOFF (p 792) show that by the end of 1942 certain improvements had been made in the preparation of typhus vaccines which rendered them more effective and that the titre of the complement fixation reaction in guinea-pigs is a reliable indication of vaccine potency. They (p 882) give information on the techniques employed in preparing these vaccines.

In a discussion at the Royal Society of Medicine (p 979) STUART HARRIS remarked that all typhus vaccine used in the British Army since 1943 was of the Craigie type and FULTON made the point that when vaccines were standardized by counting the rickettsiae it was found that animal-lung and yolk sac vaccines gave similar degrees of protection. Fox knew of no authentic case in the Allied Forces of a person dying of typhus after having been properly vaccinated with the Cox-Craigie vaccine.

GALLARDO *et al* (p 23) describe their experiences in the preparation of typhus vaccine by the Cox method.

TOPPING and SHEAR (p 457) have shown that the supernatant fluid from a centrifuged suspension of epidemic typhus rickettsiae grown in yolk sacs contains a substance having the same immunological properties (complement-fixation and production of immunity in inoculated animals) as the rickettsiae themselves. This substance is probably soluble but may possibly be contained in very small rickettsiae. [See also GIROUD below.]

ROTH (p 719) reports reactions to typhus vaccine which are probably due to residual egg antigens.

Information on delousing and immunization against typhus is contained in the *Monthly Bulletin of the Ministry of Health* (p 879). This note was intended for the information of medical men in Britain.

HORRENBERGER and RENOUX (p 107) and SERGENT and HORRENBERGER (p 365) show that sheep and goats can be used in place of rabbits for the preparation of animal-lung typhus vaccine.

By adding sterile sulphathiazole to the suspensions of infected mouse lung used in making intranasal transfers RUIZ CASTAÑEDA and ROBERTO SILVO (p 193) have been able to check secondary infections due to Gram positive organisms and have made 74 successive transfers of two strains of *R. prowazeki*. This has proved to be of great value in the preparation of bivalent vaccine.

RUIZ CASTAÑEDA and SILVA (p 457) describe experimental work which indicates that animal-lung vaccine from animals infected intranasally by both epidemic and murine rickettsiae (bivalent vaccines) are more effective against subsequent infection with epidemic strains than vaccines of epidemic origin alone.

GIROUD (p 366) shows that rickettsiae may remain alive in infected animal lungs kept at  $-25^{\circ}\text{C}$  for 14 months. There was no indication that the rickettsiae could undergo attenuation while preserving antigenic power.



GIBOUD (p. 366) has demonstrated experimentally that lung tissue in which there has been heavy growth of rickettsiae but from which the rickettsiae have been removed, possessed good antigenic properties and is effective as a vaccine.

VAISBERG *et al* (p. 549) show that the incidence of typhus in a group of medical employees who had been inoculated with a Russian mouse-lung vaccine was considerably lower than that in a comparable control group. A similar finding in other groups of people particularly exposed to infection is reported by RAVIACHICH *et al* (p. 549). When it occurred in the vaccinated, the disease was relatively mild. FAIERSTEIN (p. 456) has used a formalin vaccine from mouse lung preparations for vaccinating employees of the underground railway in Moscow. The protection afforded was moderately good.

OSBURN (p. 455) describes the preparation of an alum-precipitated vaccine from the peritoneal washings of South African gerbils infected with *R. prowazeki*. In spite of certain anomalous findings in the animal tests with this vaccine it appears to have some advantage over non-precipitated vaccines with which it was compared.

LEMAIRE (p. 268) states that the live vaccine of Blanc can be kept for an indefinite period when stocked in dry form *in vacuo*. It was used on a large scale during an epidemic of typhus in Algiers and the case incidence and fatality in the unvaccinated were 8 times and 5 times as high respectively as in the vaccinated.

CLAYTON and PÉREZ GALLARDO (p. 794) have used a "non-pathogenic and immunising strain of *R. prowazeki*" as a vaccine both in the living state and after desiccation. No serious reaction occurred in 2,217 persons vaccinated, except in one who had what might have been regarded as a mild attack of typhus. The Weil-Felix reaction becomes positive in almost half of those vaccinated. No estimate of the protective value of this vaccine is given.

BERGER and BRZEZINSKI (p. 966) have shown that the addition of petrol-ether extracts of liver or certain fatty acids to suspensions of rickettsiae has a pronounced antitoxic and antirickettsial effect.

BRAUN and UNAT (p. 108) have shown that intravenous injections of killed *Proteus O119* provoke positive Weil-Felix reactions to the same organism, and argue that mixed vaccines of rickettsiae and *Proteus* administered intravenously may be more effective than rickettsial vaccines given subcutaneously.

#### *Proteus O119 type 1 vectors: louse and flea*

##### *Louse typhus*

**Epidemiology.**—HUSAIN (p. 881) notes that louse-infestation and typhus are common in the highlands of Kashmir and JACKSON (p. 891) also refers to typhus in this area.

SOFIA and SPADARO (p. 547) claim that both the murine and the classical type of typhus exist in Amara, Ethiopia.

**Aetiology.**—ELFORD and VAN DEN ENDE (p. 455) have studied the viability and filterability of typhus rickettsiae for details the original should be consulted.

ANDERSON (p. 106) has experimented on the survival of *R. prowazeki* in milk, water and other fluids.

COHEN and CHARGAFF (p. 192) have made highly technical studies of the composition of *R. prowazeki*.

A heat labile toxin separable from the rickettsiae of epidemic and murine typhus has been studied by KENGLER and OLZEVIA (p. 23).

GIBOUD and PANTHIER (pp. 104-935) have shown that the rickettsiae of louse-borne epidemic typhus may behave either as orchitic or non-orchitic strains according to the conditions in which they are transmitted by intra-peritoneal inoculation in guinea-pigs. They have now failed to infect rats by

intrapentoneal or lung inoculation of three epidemic strains maintained in rabbit lung passages and conclude that the rat is a sure test for the differentiation of epidemic and murine rickettsiae.

PSHENICHNOV (p 269) infects lice by allowing them to feed through animal membrane on defibrinated human blood, to which an emulsion of infected louse intestine or guinea-pig brain has been added. The method of handling and rearing the lice is described by RAJKHER (p 270). SNYDER and WHEELER (p 987) have devised a technique for feeding lice on rabbits and for infecting them with typhus by this means. Infection of the lice occurred if they were fed shortly after the rabbit was inoculated, but if fed 117 hours after inoculation the results were negative. If proper precautions are taken lice may be used for the isolation of rickettsiae from patients [see LASKIN below].

**Transmission**—BLANC and BALTAZARD (p 715) demonstrated that human volunteers did not become infected when bitten by infected lice whose faeces were prevented from touching the skin. The natural reservoir of rickettsiae is infected louse faeces. GROMASHEVSKY *et al* (p 460) however contend that the only sources of infection in typhus are patients suffering from the clinical forms of the disease and the lice which have fed on them. If the spread of the disease has really been terminated it cannot again begin unless fresh cases are introduced into the community. [The authors do not support the view that inapparent cases occur and evidently do not think that infection occurs from the inhalation of dried infected, louse faeces which, in North Africa and elsewhere has been regarded as a likely source of renewed outbreaks (see PSHENICHNOV this Bulletin 1944 v 41 836)].

TOKAREVICH (p 460) describes five laboratory infections with *R. prowazeki* two by droplet infection two by contamination of mucous membranes by infected louse faeces and one by inoculation. Two of the patients had been vaccinated and the author points out that this experience was in contradiction with the consistently negative results previously obtained when feeding infected lice on vaccinated persons. The reason is perhaps related to high dosage or to maturity of the rickettsiae in these accidental infections.

By injecting into animals material from the nose mouth and trachea of patients with typhus with negative results DING (p 22) has shown that there is no direct evidence that transmission of infection from man to man can occur by droplets from the respiratory tract.

LINSKIS (p 988) reports a case of typhus contracted as a result of blood transfusion from a donor who was in the incubation period of the disease.

BLANC and WOODWARD (p 547) have shown that the monkey louse *Pediculus albidus* can become infected by epidemic typhus and that infection of ground up infected lice will transmit the disease. They have not proved that these lice can transmit typhus in natural conditions.

**Pathology**—RANDERATH (p 458) describes post mortem findings in typhus. Typhus nodules were never found in the heart which however showed a condition of typhus myocarditis. Circulatory failure was believed to be due to damage to the vasomotor centres and to be associated with the condition of the peripheral vessels rather than with myocarditis [see also the findings in scrub typhus below]. The most striking complication was diffuse haemorrhagic glomerulo-nephritis.

DURAN (p 459) describes the Fraenkel nodules of typhus. He regards the fundamental lesion of typhus as an endothelial necrosis of varying intensity. GOLDEN (p 718) gives a description of the morbid anatomy of typhus details of which should be sought in the original abstract.

AVTSYV (p 266) describes the pathological changes in the lungs of mice inoculated intranasally with suspensions of typhus rickettsiae.

**Tests**—**LASDUN** (p. 795) claims that examination of the gut of lice collected from typhus patients affords a good method of early diagnosis before the Weil-Felix test is positive. Typhus rickettsiae are present and can easily be distinguished from non pathogenic rickettsiae.

**DE LA CAMARA** (p. 984) reports an outbreak of typhus in Spain but notes that the results of the Weil-Felix test were irregular. In comment **MEDAW** emphasizes the importance of standard strains of *Proteus* and standard technique in such tests.

**FRONZKE** and **GAARE** (p. 197) have tested the specificity of the Weil-Felix reaction by the examination of a large number of sera obtained for tests for syphilis. They conclude that if a titre of 1 in 200 is accepted as a minimum, non specific reactions occur in only 1.2 per cent. of apparently uninfected persons. They conclude that in persons vaccinated against typhus and in those who have been living in infected communities the reaction may be positive possibly as a result of inapparent attacks.

**SCHROER** (p. 545) maintains that if the reagents of the Weil-Felix test are incubated together for 2 hours and then kept for 22 hours at room temperature the results in typhus are more clear-cut and there is no tendency for false positive results to develop in other diseases. The contrary view however is expressed by **WINKLE** (p. 545). The latter author (p. 546) discusses three Russian patients from the Far East who gave reactions to *Proteus* OXK and one German soldier who gave the same reaction probably as a result of infection of a wound with a strain of *Proteus*.

**NELSON** and **CRICKSHANK** (p. 383) have been unable to confirm the findings of **GRATCH** that the sera of pregnant women agglutinate *Proteus* OX19 constantly and at high titres. Similarly **HOARE** (p. 794) failed to confirm the findings of **Gratch**.

**BRUMPT** (p. 187) describes a slide test with a suspension of *Proteus* OX19 stained with methylene blue and in which a drop of the patient's blood is used, which gives results comparable with those of the Weil-Felix reaction. The test is rapidly performed and if it is done on photographic paper a permanent record may be obtained and kept.

**VARELA** (p. 364) thinks that the fact that gamepigs infected with typhus do not give a positive Weil-Felix reaction is due to the presence of an antigen in their tissues which is related to the antigen in *Proteus*.

**COHEN** (p. 981) has studied the chemical alteration of bacterial surfaces with special reference to the agglutination of *Proteus* OX19. The paper should read in original.

**VAN ROOYEN** (p. 194) has performed the rickettsia-agglutination test in 323 cases of typhus in the Middle East. In Egypt Iraq and Iran the results indicated that the epidemic strain was most common. In Palestine the murine. When the epidemic reaction was positive at higher titre than the murine the case was regarded as of epidemic louse-borne type and when the murine titre was higher as of murine type but information regarding the epidemiological conditions is seldom sufficient to justify an opinion as to which vector was concerned in a particular case. Moreover in nearly 40 instances there was only moderate difference between the titres. Some cases suggested tick-borne typhus and it is possible that this form exists there. Captured rats gave the murine reaction. The author prefers a classification by vector and would avoid the use of the words epidemic and endemic in relation to typhus. Another account of the same work has been written by **VAN ROOYEN** *et al.* (p. 284).

**RUIZ CASTAÑEDA** (p. 716) has used the rickettsia agglutination slide test in differentiation between epidemic and murine typhus with success in that agglutination of the homologous organism occurs at higher titre than that of the heterologous organism. Nevertheless cross agglutination does occur

especially with anti murine serum and epidemic rickettsiae which indicates that murine rickettsiae contain more of the epidemic antigen than *vice versa*. This may explain the greater cross protection from murine than from epidemic vaccines.

BRIGHAM and BENGTSON (p 552) show that the complement fixation test is a much more sensitive test of the occurrence of typhus in rats than the Weil Felix reaction. They support this conclusion by a large body of evidence.

WERTMAN (p 635) makes the point that when relatively crude egg yolk cultures of rickettsiae are used as antigens for complement fixation tests a non specific antigen from the yolk is present and may give false positive reactions especially with Wassermann positive sera and still more with the particularly sensitive technique of incubation for 18 hours at 4-8°C. This antigen can be removed by repeated washing and centrifugation.

DAMON and JOHNSON (p 990) prefer to carry out the complement fixation test at ice box temperature overnight rather than at 37°C for one hour.

SILVA-GONTIA (p 718) has used the complement fixation test in Mexico and concludes that the typhus there is very largely of epidemic type but that there are some cases of murine origin.

SMORODINTSEV and DROBYSHEVSKAYA (p 196) have devised a complement-fixation test for typhus designed to detect in the patient's serum an antigen which is present in the early days of the disease but which is gradually neutralized by antibodies developed by the patient so that by the 10th day it cannot be detected. Inactivated serum from the patient is mixed with inactivated convalescent serum (which presumably contains the antibody) and with titrated complement. This mixture is kept at 0-2°C for 18 hours and the sensitized red cells are then added and incubated at 37°C. Hyperimmune rabbit serum would probably give more satisfactory results than convalescent human serum. SMORODINTSEV and FRADKINA [this *Bulletin* 1944 v 41 1021] had previously described a rapid slide-agglutination test for the detection of this antigen if these two tests are confirmed their value in diagnosis in the early stages of the disease are sufficiently obvious.

LEÓN (p 984) notes that the complement fixation test with an antigen prepared from *Proteus O\19* is more sensitive than the Weil Felix reaction.

GIROUD (p 199) uses a skin sensitivity test for typhus in which an animal-lung antigen is employed. A positive result is obtained after an attack of the disease or after successful vaccination and indicates a state of immunity. A negative result is an indication for vaccination. It may occur in debilitated persons even after an attack of the disease. BISCHOFF (p 188) describes an intradermal test carried out with weak Weigl vaccine. A negative result is given in unvaccinated patients with typhus during the course of the disease and for 15 days afterwards and is taken to indicate the presence of specific neutralizing antibodies.

*Clinical features*—Clinical features of cases of louse-borne typhus are described by SINGH (p 24). The outbreak occurred in the Persia Iraq Field Force in 1943. ALCANTARA (p 988) describes the clinical features of typhus pointing out that the mildness of the disease in children which often causes it to be missed, is important epidemiologically. WU and LI (p 795) note the relative mildness of typhus probably louse-borne in South China.

WOODWARD and BLAND (p 199) have studied the cardiovascular system in typhus. They conclude that the abnormalities are due chiefly to the foci of necrosis in the smaller vessels and that there is little evidence of cardiac weakness. Renal damage is rare and the oliguria (in spite of large fluid intake) can be corrected by giving chlorides and overcoming dehydration. In treatment careful nursing and adequate fluid and supporting foods are needed. cardiac stimulants were not indicated in any case in this series. SIEDEK *et al*

(p. 105) found evidence of cardio-vascular disorders in 45 per cent. of 500 patients with typhus but these are apparently associated with damage to the vasomotor nerve centres and the peripheral vessels lesions of the heart playing only a secondary part. CHOMKO (p. 106) however has found electrocardiographic evidence of myocardial lesions.

ASCHENBRENNER (p. 104) notes that the chief cause of death in a series of cases of typhus was damage to the central nervous system. Severe myocarditis was rare. He used strophanthin in large doses during the febrile period, and in smaller doses in convalescence when evidence of circulatory disturbance persisted.

V. STOCKERT (p. 459) describes certain syndromes which result from localization of typhus lesions in various parts of the central nervous system—the mid brain bulbar and extrapyramidal syndromes. In the first the most important disturbance of the vegetative nerve centres is the characteristic fall of blood pressure but it is not certain how far myocarditis is responsible for this. SCHELLER (p. 200) has contributed a discursive paper on signs and symptoms associated with the nervous system in typhus. KOVÁCS and V. KUT (p. 481) describe the clinical features of typhus and outline a treatment which they believe to have reduced the severity of nervous symptoms and the incidence of complications.

MULLER (p. 548) describes the ophthalmological changes in typhus which include the presence of typhus nodules in the retina or choroid, and retinal haemorrhages.

ASCHENBRENNER (p. 25) remarks on the very great increase in blood urea which may be a feature of typhus. He is unable to explain it except as due to increased production of urea and diminished excretion owing to renal damage either inflammatory or functional.

WILCKENS (p. 266) describes the symptoms of typhus noting that an after fever lasting 1-2 days is relatively common. In treatment he found that administration of luminal was of some benefit. ASCHENBRENNER & MARX (p. 105) note that an unexplained rise of temperature may occur during convalescence from typhus. They also give a list of the common complications of the disease.

RAETIG (p. 25) describes two cases in which, he claims, true relapse occurred after attacks of typhus. In comment MEGAN throws doubt on the diagnosis of the first febrile attack in each case. It is noted that each of these patients was treated by injection of convalescent serum and the question arises whether each was in fact infected by the serum.

*Treatment*—LEOMANS *et al* (p. 201) report encouraging results in a small series of typhus patients treated with *p*-aminobenzoic acid in the first few days of the attack and compared with a series of comparable controls. The optimum dosage is not known but the initial dose was 4-8 gm. followed by 2 gm. every 2 hours until the temperature was normal. The drug was given suspended in 5 per cent sodium bicarbonate solution. The effect of this treatment was to shorten the febrile period and to reduce the severity of the disease. Some of the treated patients had a secondary rise of temperature soon after the end of drug treatment this was not serious. The effect of *p*-aminobenzoic acid, both in inhibiting the growth of rickettsiae in yolk-sac culture and in treatment of mice infected with a murine strain, was demonstrated by GREIFF *et al* (p. 382). PRINCEPOTON (p. 878) also discusses the therapeutic action of *p*-aminobenzoic acid in typhus. HAMILTON *et al* (p. 786) describe the inhibitory action of *p*-aminobenzoic acid on rickettsiae (epidemic and murine strains) growing in yolk sacs of fowl embryos.

LEÓX (p. 202) has used hyperimmune rabbit serum for the treatment of typhus giving 20 cc. intravenously at intervals of 12 hours until the temperature subsides. The results were apparently satisfactory in a small series of

cases. A beneficial effect of the use of hyperimmune rabbit serum in louse typhus is also indicated by the results obtained by STEVENS (p 364) in a small series of patients. SHUBLADZE *et al* (p 461) have immunized horses with infected mouse-lung preparations of *R. prowazeki* and have used the horse sera for treatment of typhus in animals with some success. Preliminary clinical trials in man have been promising.

Certain substances which are described in the original abstract were tested for activity against the rickettsiae of murine and epidemic typhus by ANDREWES *et al* (p 20). Activity was recognized in some of these drugs but they proved disappointing in the treatment of human typhus. SKORIN and KORSHUNOVA (p 638) have tested 56 compounds for chemotherapeutic activity in experimental typhus. In a critical evaluation of the many drugs which have been advocated by German medical men BRANDENBURGER (p 28) adopts an attitude of scepticism. He relies on careful nursing and the administration of plenty of fluid, with generous and varied diet.

Treatment by daily warm baths, injections of artificial blood and saline is advocated by LAMPERT (p 365) but the evidence of its value is not clear.

YARYGIN and NAGIBINA (p 989) describe the method of buxation which consists of alternately withdrawing and reinjecting 10 cc. of cerebrospinal fluid after the patient has been given large doses of sodium salicylate. This treatment (for details of which the original abstract should be consulted) was tried in typhus with some favourable results.

ALISOV and KOSSOVAJA (p 989) have observed some benefit from vaccine therapy in severe attacks of typhus.

LAURE (p 267) describes the types of gangrene seen in typhus and the treatment advocated, which consists of infiltration of the lumbar sympathetic ganglion with novocaine without adrenaline.

**Control**—SERGENT and BÉGUET (p 270) have used the insecticide powders MYL and DDT for delousing certain communities in Algeria. These preparations were very effective but the authors are pessimistic on the question of complete and permanent eradication of lice and conclude that these dusts can best be used by mobile disinfecting units when outbreaks of typhus occur.

BEACH and RENNIE (p 880) report four cases of typhus in prisoners of war returned to England from Germany. They had been dusted with DDT and were free from lice. MEGAW in comment makes the point that delousing by DDT does not sterilize infected louse faeces.

### *Louse and flea typhus*

LEON (p 193) argues that typhus is caused by a single species of rickettsia of which there are two strains [2 varieties] *R. prowazeki prowazeki* and *R. prowazeki mooseri*. The former does not provoke vaginitis in animals; the latter does so. Either strain can cause endemic or epidemic typhus and either can be of high or low virulence. The author supports his conclusion by records of his own work. In comment MEGAW points out that although these organisms cannot be clearly differentiated by their capacity to provoke orchitis they can be distinguished by complement fixation and rickettsia-agglutination tests. From the point of view of control, the vector louse or flea is important.

SILVA and RUIZ CASTAÑEDA (p 990) having infected guinea-pigs with both epidemic and murine rickettsiae simultaneously have found that transfers through male guinea-pigs favour the isolation of the murine strains and through females of the epidemic strains.

ANDERSON (p 192) has shown that the cotton rat *Sigmodon hispidus hispidus* is as highly susceptible as the South African gerbil to infection with classical

and murine strains of typhus rickettsiae it has therefore been used in laboratory research work. Sera of infected cotton rats do not agglutinate *Proteus* OX19.

### *Flea typhus*

SOFIA (p. 109) has isolated rickettsiae of the murine type from man in Asmara (Eritrea) and also from the brains of wild rats. HARRINGTON and YOUNG (p. 271) have isolated murine strains of rickettsiae from rats and from a patient in South Africa, near Port Elizabeth.

POLLARD and AUGUSTOV (p. 551) perform complement fixation tests on rats to detect evidence of murine typhus in them. They have obtained positive results in endemic areas but not where the disease is not known to occur. Some of the rats giving positive tests were captured in theatres—this fact may explain certain outbreaks in man.

IRONS *et al.* (p. 462) have isolated murine rickettsiae from *Ctenocephalides felis* from kittens probably connected with a human outbreak. It is possible but unlikely that the fleas acquired the infection from rats and the present finding indicates that cats may be a reservoir of infection in certain circumstances.

According to evidence collected by REIZ SÁNCHEZ (p. 272) the endemic typhus of Guadalajara, Mexico is of murine origin. VARGAS (p. 766) has isolated a strain of murine rickettsiae from a patient in El Salvador. MACCHIAVELLO (p. 103) has studied strains of rickettsiae isolated from patients or from lice in Ecuador. One of these was regarded as a murine strain but the other two behaved irregularly in animals. The author does not think that the terms orchitic and murine as applied to strains of rickettsiae are synonymous. MONTORYA (p. 551) reports an outbreak of typhus which he thinks was murine in origin in Colombia.

ALICATA and BREAKS (p. 271) have isolated rickettsiae from a patient in Honolulu which were identical with a standard murine strain, and from a high proportion of rats in the area. Cats, dogs and the fleas collected from them were negative.

LIU (p. 719) has isolated rickettsiae of murine type from rats, rat fleas and lice during an outbreak in Perang. He thinks the human disease may have been louse-borne but MEGAW, commenting on this, is not convinced that louse-transmission was conclusively proved.

JETTMAR and SHIGAN (p. 881) report on the Weil-Felix reaction in man and rats in Kweichow, China.

BLANC *et al.* (p. 713) have shown that the ass-louse *Haematopinus asini* may transmit murine rickettsiae and *Xenopsylla cheopis* and *Pulex irritans* epidemic rickettsiae. The fleas *X. cheopis* and *Ctenocephalides canis* do not appear to be able to transmit the rickettsiae of Rocky Mountain and boutonneuse fevers.

DIXON and JOHNSON (p. 637) compared freshly prepared rickettsial suspensions (epidemic or murine types) with commercial vaccines in relation to their usefulness in the complement fixation test for typhus of murine type. The best results were obtained with the fresh suspension of the murine type.

ARBOVA (p. 990) quotes evidence which suggests some slight favourable effect in the treatment of flea borne typhus with mepacrine.

### *Proteus* OXh type I vector mice

MEGAW (p. 797) has contributed a comprehensive account of scrub typhus, in which he shows that during the war there has been an average case-mortality rate of 10–15 per cent, a high incapacitation rate and a depressing psychological effect. He discusses classification, epidemiology and transmission and in relation to the clinical findings makes the point that a necrotic ulcer is not

always present. No adequate summary of this paper and of the comments of LEWTHWAITE who reviewed it is possible in brief space and the original should be consulted. It was a timely account of an important disease.

FARNER and KATSAMPES (p 272) have compiled a summary of available information on tsutsugamushi disease which should be read in the original.

DE VIDAS (p 882) describes the clinical and pathological features of scrub typhus as he saw it in New Guinea noting that the maximum titre of the Weil-Felix reaction with *Proteus* OXA occurred 22-25 days after onset. SATHER and SILBERSTEIN (p. 885) also report on cases from New Guinea.

SINGH (p 883) gives an account of an outbreak of scrub typhus in Burma in soldiers who had camped in a rural area. MENON and IBBOTSON (p 884) record an outbreak in a unit which entered a typhus island in N.E. Burma. Clinical features and complications are described, and treatment is outlined. The authors note that malaria was so common that a therapeutic course of mepacrine was given at the onset in all cases.

HAY (p 109) describes an outbreak of scrub typhus in a force of Royal Marines who landed on an unnamed coast in the Far East. These men had been working in close contact with scrub conditions. The symptoms are described, but the description should be sought in the original abstract. Primary lesions once thought universal in this disease were rare. Diagnosis was confirmed by agglutination of *Proteus* OXA in high titre in all cases. It was found that local inhabitants also gave positive reactions with *Proteus* OXA and it seems probable that all local children become infected at some time and that local adults possess some degree of immunity. Larval mites probably *T. deliensis* were found on trees and grasses and on rats chiefly *Rattus rattus frugivorus*. Serological tests on rats indicated that the disease was present in them. Later evidence (MANSON *J. Roy. Soc. Med. Ser.* 1946 v 32 105) makes it clear that this outbreak also referred to by ZAIR (below) occurred in the Maldive Islands.

WILLIAMS (p 367) has published a list of mite vectors and animal reservoirs of tsutsugamushi disease. [The evidence available for some of the mites mentioned is somewhat tenuous. The mites definitely incriminated in the literature appear to be —

*Trombicula akamushi*

*Trombicula deliensis*

*Trombicula fletcheri* (probably = *T. akamushi*)

*Trombicula walchi* (probably = *T. deliensis*)

In addition *T. minor* (= *T. hirshi*) is suspected.]

BLAKE *et al.* (p 991) made a very thorough study of tsutsugamushi disease in New Guinea. They point out that the only mite hitherto proved by experiment to be a vector is *T. akamushi* though there is much evidence to incriminate *T. deliensis*. The only animals so far found infected in nature are the vole *Microtus montebellii* and undetermined species of wild rats in Malaya. They isolated strains from *Trombicula fletcheri* [= *akamushi*] which were identical with those isolated from man. The Syrian hamster was found to be specially suitable for passage. The authors give descriptions of the disease in man. This long monograph should be read in original. KOHLIS *et al.* (p 993) report a continuation of the same work in which they recovered *R. orientalis* from pools of *T. fletcheri* [= *akamushi*] and *T. walchi* [= *deliensis*]. These were taken from *Rattus concolor browni*. The rickettsiae have also been recovered from this rat.

McCULLOCH (p 369) makes the point that all the species of mites which occur in countries in which scrub typhus is endemic should be regarded as potential vectors of that disease. [Such a view needs verification.] He describes their



habits and the means of controlling them. WOMERSLEY and HEADLIP (p. 28) have written a comprehensive paper on the Trombiculinae of the Austro-Malayan and Oriental Regions. No further abstract of this is possible.

From his experience of three outbreaks of scrub typhus COOK argues that the possibility should be entertained that this disease may be transmitted by ticks (as has previously been suggested by workers in the Netherlands East Indies).

In Ceylon, LUCAS (p. 888) has isolated a strain of *R. tsutsugamushi* [*R. orientalis*] from man by passage through guinea-pigs, white rats and white mice. He considers the white mouse to be the animal of choice for this work. VAN ROOYEN and DAKSIN (p. 483) note that two species of Egyptian gerbils and the jerboa are extremely susceptible to the rickettsias of scrub typhus.

SYVERTON and THOMAS (p. 879) describe a method of staining *Rickettsia tsutsugamushi*.

HICKS (p. 554) describes the post mortem findings in scrub typhus. The chief histological changes were proliferation of the reticulo-endothelial tissues and infiltration of interstitial tissues with mononuclear cells, especially in the heart, lungs and spleen. The naked-eye changes are described.

WILLIAMS *et al.* (p. 369) give a detailed account of the clinical features of scrub typhus drawn from an experience of 626 cases. The original abstract should be consulted for details, but it may be mentioned that the value of the Weil-Felix reaction with *Proteus OXK* was confirmed, provided the strain of *Proteus* is suitable, that an eschar was seen in only 59 per cent. of the cases, that the death rate was profoundly influenced by lowered resistance due to hardship, malaria and dysentery, and that there was no evidence of permanent cardiac disability in those who recovered.

LIPMAN *et al.* (p. 371) also describe the clinical features of scrub typhus, and the original abstract of this paper also should be consulted for details. They give a list of complications in which cardiovascular disturbances are prominent. A similar description is given by BERRY *et al.* (p. 535) who regard the vascular changes found at post mortem to be of primary importance, myocardial and pulmonary lesions being secondary to them. They note that obstinate cardiac neurosis may occur if any suggestion of heart disease is made to the patient. LEVINE (p. 556) also stresses the fact that suggestion of heart disease may make an almost ineradicable impression on the minds of people suffering from scrub typhus leading to neuro-circulatory asthenia. In actual fact there were only two cases of true cardiac disease in 130 patients.

A comprehensive description of the clinical features of scrub typhus is given by MACHELLA and FORRESTER (p. 864).

In *Army Medical Department Bulletin* No. 41 (p. 112) there is a note on fluid retention in scrub typhus. This is a common feature of the disease and is often relieved by diuretics which occurs relatively suddenly about the 14th day of disease, this is associated with subjective improvement and is usually followed by reduction of the fever.

A study of the blood chemistry in scrub typhus is reported by GOTTFRIED (p. 885). The details are numerous and should be sought in the original abstract.

WEND (p. 111) reports an increase in speckled lymphocytes in the convalescent stages of scrub typhus which is seen only rarely in other diseases. The cells are described, and it is noted that speckling occurs in a proportion of lymphocytes in normal blood.

LOGUE (p. 274) describes an outbreak of mite typhus among American troops on an island in the S.W. Pacific and outlines the preventive measures which, when adopted, were successful. These comprised preparation and treatment of camping sites, rat control, the use of dimethyl phthalate and insecticidal powder. [In the abstract the word *kural* is a misprint for *kurus* grass.]

In an outbreak of scrub typhus in the south Pacific the incidence declined sharply after certain control measures were instituted —trapping of rats cutting and burning of *Kunai* grass spreading of sand wearing of leggings and the liberal use of repellents (MOREHEAD p 720) In the *Journal of the American Medical Association* (p. 799) is a note to the effect that the United States forces have substituted benzyl benzoate for dimethyl phthalate for the impregnation of clothing as a protection against mites.

In the prevention of scrub typhus among men engaged in clearing scrub ZAIR (p. 111) notes that bulldozers are useful for this purpose and that if manual clearing is necessary the scrub should first be sprayed with kerosene and burned. Advice is given in regard to rat-control operations.

LEWTHWAITE (p 980) refers to the immunity conferred by an attack of tsutsugamushi disease

STEPHENSON (p 553) reports a single case of fever of the typhus group with a strong reaction to *Proteus OXA* in the Sudan where mite-borne typhus is not known

#### *Indeterminate type Vector tick*

MARIOTTE *et al* (p 721) report natural infection of *Rhipicephalus sanguineus* with rickettsiae of Rocky Mountain fever in Mexico BUSTAMANTE and VARELA (p 203) have found Rocky Mountain spotted fever in rural areas of Mexico The vector was probably *Rhipicephalus sanguineus*

PLOTS *et al* (p 636) have tested the sera of persons with Rocky Mountain spotted fever by the Weil-Felix complement fixation rickettsia agglutination and mouse neutralizing tests to find a satisfactory means of differentiating this disease from epidemic and murine typhus The Weil-Felix results were irregular as is usual in tick borne typhus and the rickettsia agglutination test did not afford good differentiation The complement fixation reaction gave uniformly consistent results with clear-cut differentiation It was found that antibodies capable of neutralizing epidemic and murine toxins were present in Rocky Mountain spotted fever [See also WOLSTENHOLME and GEAR above.]

HARRELL *et al* (p 373) challenge statements which have been made to the effect that intravenous medication does more harm than good in Rocky Mountain spotted fever and they claim that the collapse of the peripheral circulation which occurs corresponds to the condition of shock and may need treatment with plasma or blood. The administration of fluid should be very carefully controlled as to amount and type—saline and glucose or blood. The same authors (p 888) think that in Rocky Mountain fever as in burn shock there is extensive leakage of proteins through the walls of blood vessels into the tissues. They treat their patients therefore with transfusions of plasma one effect of which is to promote the reabsorption of crystalloids into the vessels. This treatment is carefully controlled by estimation of non protein nitrogen, serum proteins and chlorides of the blood. A high-protein diet is useful.

The action of *p*-aminobenzoic acid in guinea-pigs infected with Rocky Mountain fever appears to be purely suppressive but it prevented death in many of the animals though all controls died (ANIGSTEIN and BADER p 888)

EDMONDS (p 464) has treated one patient suffering from Rocky Mountain spotted fever with penicillin. This was apparently very successful but no value was found by FITZPATRICK (p. 996) in the treatment of experimental Rocky Mountain spotted fever with penicillin.

HEILIG and NAIDU (p. 30) refer to the fevers of the typhus group which have been seen in the State and City of Mysore and to the complement-fixation tests carried out on some of these cases by TOPPING. The results of these tests

indicate that the disease is related to Rocky Mountain spotted fever rather than to other members of the typhus group. Cases of some fever of the typhus group but without rash, are described from the United Provinces of India by BARDHAN (p. 29). PRADHAN (p. 29) describes cases of a typhus-like disease, possibly transmitted by ticks which he has seen in recent years in Berar, India.

PESTANA (p. 638) gives reasons for his view that the typhus of São Paulo may not entirely be of the Rocky Mountain type but may include cases of the flea borne murine type.

PATISCO-CAMARGO *et al.* (p. 799) proved that an adult *Ornithodoros parkeri* contained living rickettsiae 1 087 days after a feed on a guinea-pig with the spotted fever of Tobia. A related species *O. rufus* is a potential vector and is abundant in Tobia.

DE MAGALHÃES and ROCKA (p. 886) have produced inapparent infection in certain common Brazilian small animals by injection of infective material from Brazilian exanthematic typhus. They describe the clinical types of this disease. [This form of typhus is presumably tick borne.] The same authors (p. 988) have tried penicillin in Brazilian typhus [tick borne] there seems to be some slight beneficial effect.

RODHAÏM and BARLOVATZ (p. 887) discuss the histology of the eschar in the disease found in the Belgian Congo which resembles boutonneuse fever. An outbreak of tick typhus in East Africa is described by WALSH (p. 720) in which a local lesion was found in every case.

CAVAZZI (p. 113) has seen five cases of boutonneuse fever in the Ethiopian highlands.

KORSHUNOVA *et al.* (p. 274) give an account of tick typhus as it occurs in central Siberia. The infection is apparently found in ground squirrels and other rodents and is transmitted to man by *Dermacentor nutalli* and possibly by other ticks. A strain isolated from man immunized animals against Marseilles (? boutonneuse) fever. SHKORBATOV (p. 484) discusses tick-borne typhus in the far east of the Soviet Union where the vector appears to be *Dermacentor sibiricus*. Serum reactions are most commonly given to *Proteus* O:19.

#### Bullis fever

BADER and ANIGSTEIN (p. 639) report their experiments to determine the specificity of the rickettsiae isolated from *Amblyomma americanum* and from a patient with Bullis fever. The strains are not related to Q fever or Rocky Mountain spotted fever. The details of the experiments should be sought in the original abstract but in comment MEGAW remarks that perhaps more than one short tick-borne fever may have been included under the name Bullis fever. BLAIR and BADER (p. 709) have induced fever in nine volunteers inoculated with material derived either from patients with Bullis fever or from infected ticks and subsequently passaged through guinea-pigs. Many other attempts to infect man were unsuccessful. LIVERAY and POLLARD (p. 203) have carried out complement fixation tests on patients recovered from Bullis fever using an antigen prepared from the spleens of infected mice. Most of the tests were positive. Control tests were negative. Sera from certain animals shot in the neighbourhood were also positive.

BRENNAN (p. 799) gives a list of ticks and vertebrates at Camp Bullis. Some of these may perhaps be important in relation to Bullis fever.

#### Trench fever

In a discussion of trench fever v. BORMANN (p. 462) states that abortive attacks are common that shin-bone pains have little diagnostic value and that less than one-third of the attacks in one outbreak were of the periodic

type A pronounced leucocytosis with relative lymphocytosis is a feature of the febrile periods of trench fever with a return towards normal during the afebrile intervals (BIELER p 204) HELD (p 113) describes nodules resembling rheumatic nodules in the scalp and the skin of other parts of the body which he believes to be the physical basis of the headaches shin-bone pains etc of trench fever

REUTER (p 204) describes trench fever

KIBLER (p 639) notes that there may be difficulty in differentiating trench fever from influenza, paratyphoid typhus and wound sepsis The clinical features are very variable He points out that the blood may be infective for a long time and that it is therefore unsafe to use the patient as a blood donor for two years after the attack

REUTER and SCHÄFER (p 204) think that war nephritis and trench fever are variants of the same disease largely because the periodicity and the pains are of the same type and because nephritis often occurs in trench fever

Solustibosan has been found useful in the treatment of trench fever (EBERLIN p 31) BEIGLBÖCK and LOSCHER (p 31) have treated trench fever with Pvrifer a colon bacillus vaccine with some benefit Charles H Wilcocks

## MALARIA

MACARTHUR, W. A Brief Story of English Malaria. *Post-Graduate Med J* 1946 July, 22, No 249 193-200

SEZONISMO Lisbon. Dez anos de luta contra a endemia [Ten Years of Antimalarial Work in Portugal.] 169 pp. (Publicação da Direcção de Serviços Anti Sezonáticos 1942.)

— A luta contra a endemia no ano de 1941 [Antimalarial Work in 1941] 176 pp (1942.)

— A luta contra a endemia no ano de 1942. [Antimalarial Work in 1942.] 230 pp (1943)

— Trabalhos originaes-1942. [Original Papers, 1942.] 212 pp (1943)

— A luta contra a endemia no ano de 1943. [Antimalarial Work in 1943.] 239 pp. (1944)

— Trabalhos originaes 1943 [Original Papers, 1943] 90 pp (1944)

This publication is issued each year by the Ministry of the Interior Public Health Department Lisbon, and is a record of the antimalarial activities of the previous year The word *Sezonismo* was used for malaria by Ricardo JORGE who though not the originator of the Portuguese antimalaria organization was well known for his work on the subject.

The first number of *Sezonismo* issued in 1942, contains an account of 10 years of this work up to 1940 The later numbers cover the years 1941 1942 and 1943 separately Those who wish to follow the malaria investigations in Portugal should consult these publications

In addition to this general account of routine work, a separate publication with the same name is issued each year and contains original papers of work done in the previous year

Charles Wilcocks

PAPAFIOGOU Th. *Deux cas d'infection à P. ovale Stephens en Grèce* [Two Cases of Infection with *P. ovale* in Greece.] *Rev. Paludisme et M. Trop.* 1946 June 15, v. 4, No. 27 180-83 10 figs. [12 refs.]

CORRÊA R. R. *Sobre a incidência da malária, em especial do Plasmodium malariae (Laveran, 1881) no Ramal de Itapura* [The Incidence of Malaria, especially *P. malariae* in the Ramal de Itapura, Brazil.] *Arquivos de Hig. e Saúde Pública* 1945 Dec. v. 10 No. 28, 181-7 3 figs. on 1 pl. & 1 map [17 refs.] English summary

CODA D. *Malária quartã no litoral sul* [Quartan Malaria in Iguaçu, São Paulo State, Brazil.] *Arquivos de Hig. e Saúde Pública* São Paulo 1945 Sept. v. 10 No. 23 79-80 English summary (3 lines)

MARTINS A. V. & VERRIANI V. *Novo foco de malária quartã no estado de Minas Gerais* [A New Focus of Quartan Malaria in Minas Gerais.] *Brasil Medico* 1946 May 4 & 11 v. 60 Nos. 18/19 168-9

RIBBANDS C. R. *Effects of Bush Clearance on Flighting of West African Anophelines.* *Bull. Entom. Res.* 1946 May v. 37 Pt. 1 33-41 2 figs.

The experiments described in this paper were conducted in an attempt to discover if the eradication of low vegetation around human dwellings reduced the numbers of anopheline mosquitoes attracted to them.

The main work was done at a village near Sekondi, Gold Coast between January and March 1942. In this village all but three of the huts were pulled down—the observer used one of them and seven Africans were installed in the other two. There was a large swamp 850 yards to the east. To allow for any differences in individual attraction to mosquitoes the Africans were regularly changed about. Daily catches of mosquitoes were made in the two huts between 7 a.m. and 9 a.m. and night catches were made in one of them. These, the experimental catches, were compared with simultaneous control catches made in three other huts: one the "inner control" hut 100 yards away was newly erected for the experiment in the direction of the swamp and was occupied by three Africans. The other two the outer control huts were already established in a south easterly direction: one at 650 yards distance occupied by three Africans and one at 850 yards occupied by one African. The catches in these two huts were averaged. After three weeks the bush was cleared around the two experimental huts for an average radius of 140 yards; this work took five days. Catching continued during this time and for another three weeks.

Counts of anopheline mosquitoes caught in the experimental huts were calculated as percentages of the corresponding counts in the control huts. These figures are presented graphically and in tables in three groups—before, during, and after the bush clearance. They show little difference between the proportion of female *A. funestus* and *A. gambiae* caught in the experimental huts after the clearance, and the proportion which reached the huts before the clearance: males entered in the same proportion as before. During the clearing operations the proportion of females dropped to nearly a quarter and of the males to one-half of that before the clearance: this reduction is attributed to the masking of the scent of man by the odour of the cut decaying vegetation.

A somewhat similar experiment had already been made during August and September 1941 at Aberdeen near Freetown Sierra Leone, where the predominant anopheline was *A. melas*. Catches were made for 14 nights in seven huts: six of them in a clearing and the seventh 25 yards from the others but ten yards inside the bush which reached 15 ft. in height. The African occupants

changed huts in rotation. Catches made in the bush hut were compared with those made in the nearest hut in the clearing and though there were variations on different nights the bush hut provided an average nightly yield for the 14-day period of 47.4 per cent. of the total catch.

There are features about these experiments which may appear to be unsatisfactory to the reader such as the number of Africans, number size and age of huts but the author believes that the results indicate that bush clearing around dwelling places is not justified as a measure for reducing anopheline infestation—a conclusion which is meant to apply only to *A. gambiae* and *A. fimestus* in West Africa.

H S Leeson

VARGAS L. Consideraciones sobre el complejo del *Anopheles pseudopunctipennis* [Studies on the *A. pseudopunctipennis* Complex.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Dec. v 6 No. 4 265-70 1 fig. [15 refs.] English summary

The *Anopheles pseudopunctipennis* complex studied up to now discloses the following subspecies: *typicus* Theobald 1901, *franciscanus* McCracken 1904, *bovdi* Vargas 1939 and *willardi* Vargas 1941. The author mentions the most remarkable morphological data useful in the identification of these. The subspecies *typicus* acquires importance in the transmission of malaria only when the high numbers of individuals form a large population.

CORRÊA R. R. Da infecção natural pela plasmodiose malarica do *Anopheles (Kertessia) cruzi* D. H. 1908. Natural Infestation with Malaria of *A. cruzi*. *Folia Clin et Biol São Paulo* 1943 v 15 No 1 23-32, 11 figs. [11 refs.] English summary

FOXSECA J. A. B. & UXTI O. Infecção experimental de anofelinos de regiões endêmicas à malária. [Experimental Malarial Infection of Anophelines from Areas of Endemic Malaria.] *Folia Clin et Biol São Paulo* 1943 v 15 No 1 43-52.

BRIGGS G. D. S. A Case of Cerebral Malaria on Board a Troopship. [Memoranda.] *Brit Med J* 1946 July 13 51-2.

MARSHALL, E. H. JR. Chemotherapy of Malaria, 1941-45. *Federation Proc Baltimore* 1946 June v 5 No 2 298-304 [15 refs.]

ENGLISH J. P., CLARK, J. H., SHEPHERD R. G., MARSON H. W., KRAPCHO J. & ROBLIN R. O. JR. Studies in Chemotherapy. XIV. Antimalarials. The Synthesis of Substituted Metanilamides and Related Compounds. *J Amer Chem Soc* 1946 June v 68 No. 6 1039-49 4 figs. [Refs in footnotes.]

ANY TROP MED & PARASIT 1946 Apr v 40 No 1 80-87 7 figs on 2 pls. The Effects of Mepacrine on the Gastro-Intestinal Tract of Man. [Army Malaria Research Unit Oxford (MAGGRAITH B. G. *et al*) & Nuffield Institute for Medical Research, Oxford (FRANKLIN K. J. *et al*)]

Mepacrine was given to numerous volunteers in various doses and one and a half hours later they were given a barium meal so that the movements of the alimentary canal could be observed radiologically. Twelve women received single doses of 0.6-1.0 gm. mepacrine. Clinically they experienced headache, often severe, nausea, sometimes repeated vomiting, colicky abdominal pain and diarrhoea. In more severe cases, fever and prostration occurred. These symptoms began to disappear after 8-9 hours. Radiologically immediately

after the taking of the barium meal there was gastric hypersecretion, hyperperistalsis increase of tone of the pyloric antrum followed by atony and pylorospasm. Emptying of the stomach was delayed. The intestines were abnormally active and the rate of passage of the meal along them was increased, although there was delay at the ileo-caecal valve. Once the meal entered the colon it advanced very rapidly there was also marked outpouring of secretion in the colon. The gall bladder appeared normal, and no significant change could be detected in the flora of the faeces.

On the other hand a large number of volunteers on a suppressive régime of 0.1 gm. mepacrine daily rarely showed gastro-intestinal disturbances, and such disturbances as did occur were slight or unimportant. Fractional gastric analyses were carried out on the second day of taking 0.1 gm. mepacrine but they revealed no significant abnormality. In 12 volunteers gastroscopy was performed. The gastric mucosa as a whole was normal, but immediately around the site of the tablet there was hyperaemia, and the accumulation of thick mucus but this effect was too slight to explain the symptoms which are sometimes experienced. Two patients with quiescent chronic ulcerative colitis received 0.1 gm. mepacrine daily for a fortnight there was no change in their general condition or in the bacterial flora of the stools.

It is recalled that widespread disturbances especially vomiting and diarrhoea, occurred among the troops in North Africa in 1943 when they were given 0.2 gm. mepacrine twice weekly. The symptoms occurred most frequently after the third dose developing 3-10 hours after the dose had been taken. Investigations at the time had shown that they were not psychogenic, they were not due to abnormally toxic batches of mepacrine and they were not due to some bacterial infection. In the present investigation eight volunteers were given 0.2 gm. twice weekly. Six volunteers showed no ill-effects two volunteers experienced severe symptoms after the third dose resembling those seen in North Africa. The concentration of mepacrine in the plasma of these two volunteers was within normal limits. It is concluded that when a dose of mepacrine is repeated at intervals greater than two days the tolerance for mepacrine in some of the subjects may be reduced by the time the third dose is given, and that such a régime should never be used. F. Hacking

MANDEKOS, A. G. [D.D.T. (Neocid, Gexarol, Gix) A New Insecticide which will revolutionise the Methods of controlling various Diseases transmitted by Insects.] *Helleniatr Salonica* 1945 repr. 16 pp. [In Greek. English summary.] [Summary taken from *Rev. Applied Entom.* Ser. B 1946 June v. 34 Pt. 6 99.]

From laboratory and field experiments carried out in Greece in 1943 and 1944 it is concluded that Neocid (5 per cent. DDT in talc) is effective against larvae and adults but not eggs or pupae, of *Anopheles* and *Culex*. Contact with the powder or with a suspension of 1-6 gm. Neocid in 1,000 cc. water with the addition of 2 cc. kerosene caused adults and larvae to die in 3-4 hours. Ceilings and walls of bedrooms or stables can be kept free from mosquitos for at least five weeks by the application of 1 gm. Neocid in 2 cc. kerosene and 18 cc. water per sq. metre [4.65 mg. DDT per sq. ft.]. A suspension of 2 gm. Neocid and 2 cc. kerosene in 1,000 cc. water applied at 70 cc. (7 mg. DDT) per sq. metre [about 1 oz. DDT per acre] to breeding places of races of *Anopheles maculipennis* Mg. including var. *saravorei* Fabr. (*clutus* Edw.) gives very good initial kill but an application must be made every week. In the fast flowing streams in which larvae of *A. superpictus* Grassi occur better results are obtained if a larger quantity of Neocid is used (160 cc. of a suspension containing 5 gm. Neocid and 10 cc. kerosene per 1,000 cc. water). In 1944

this dosage was used in breeding places in Salonica and the total number of Anophelines taken in ten catching stations in the city and its outskirts was 85 compared with an average of 69.1 and a range from year to year of 38.8 to 166.5 in 1939-43 when Paris green was applied by a dustless method. Comparative figures are given showing the amounts of DDT required per unit area for spraying walls or treating breeding places by the methods of application described by the author and by Smith.

BRUMPT E. Grande utilité de deux plasmodies aviaires *Plasmodium gallinaceum* Brumpt 1935 et *Plasmodium lophurae* Coggeshall 1938 pour l'étude scientifique et pratique du paludisme humain. [The Great Value of *P. gallinaceum* and *P. lophurae* for the study of Human Malaria.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Dec v 6 No 4 199-203

## TRYPANOSOMIASIS

STEWART J. L. Eradication of *Glossina* in the Naboggo Valley, Gold Coast. *Bull Entom. Res* 1946 May v 37 Pt 1 99-103

Animal trypanosomiasis made it impossible to keep any cattle except the relatively resistant and inferior local dwarf breed in the Naboggo valley. The tsetse present consisted of *Glossina palpalis* and *G. tachinoides*. The fly appeared dependent on the bush fringing the river, a meandering stream which is converted into separate pools in the dry season (November to June). The fringing bush in this whole valley was cleared selectively. Experiment showed that only the trees fringing the water need be removed; these were cut at the beginning of the dry season and the stumps completely burned in May. This needed supervision but with care gave excellent results, maintenance of the clearing proved practicable.

Erosion after clearing was feared but the river never flows rapidly and the quick and profuse growth of grass in cleared areas held the soil together. Some damming was done to conserve water for domestic use and for irrigation as well as to prevent erosion.

The economic value of the work was soon manifest. The valley was able to maintain a much larger population of cattle of superior breeds (susceptible to trypanosomiasis).

Kenneth Mellanby

TRYPANOSOMIASIS COMMITTEE OF SOUTHERN RHODESIA. The Scientific Basis of the Control of *Glossina morsitans* by Game Destruction. *Rhod Agric J* v 42 No 2 124-8 also as *Bull Minist. Agric.* [S Rhodesia] No 1303 6 pp Salisbury S Rhodesia 1945 [Summary taken from *Rev Applied Entom.* Ser B 1946 June v 34 Pt 6 103-4]

Measures have been taken in Southern Rhodesia during the past 25 years to create and maintain game-free zones in order to prevent the extension and ultimately cause the retrogression of *Glossina morsitans* Westw. The regular hosts of *G. morsitans* are the larger grazing and browsing mammals available all the year round and it also has occasional hosts which are nocturnal exceptionally active migratory or seasonally hidden by long grass. It must obtain meals at regular intervals to replace water lost by evaporation. The extermination of most of its usual hosts deprives it of opportunities of obtaining regular meals and forces it to expend energy seeking other sources of food and thus lose much moisture so that the death rate rises far above normal and



females may abort. To eliminate *G. morsitans* from an area, therefore it is not necessary to exterminate every species of animal on which it can feed—it is sufficient to eliminate those that provide a dependable source of food throughout the year. When this has been done the fly cannot support life when grass is high and dense. As *G. pallidipes* Aust. can find its prey even in thick vegetation game destruction has to be very drastic to be successful by itself in eliminating this species. If a zone that has been freed of *G. morsitans* has its ends in fly-free country or is 50 miles or more long game can be allowed to re-enter it by moving the shooting zone forward into the fly belt without increasing its width (10–20 miles). The desirability of doing this is discussed. It is pointed out that the presence of much game in a cattle area results in loss of pasturage and increases the difficulty of controlling tick borne and other diseases of stock and that certain species destroy crops or are a menace to human life.

RODHAEM A. J. Documents pour servir à l'histoire de la maladie du sommeil au Congo belge (Deuxième note) La trypanosomiasse humaine dans le district de l'Aruwimi en 1907 et en 1908. [Documents relating to the History of Sleeping Sickness in the Belgian Congo. 2. Human Trypanosomiasis in Aruwimi District, 1907–08.] Inst Roy Colonial Belge—Bull des Sciences 1946 v 17 No 1 368–79 1 folding map

FLOCH H & DE LAJUDIE P. Recherches sur la trypanosomiasse humaine américaine en Guyane française. *Rhodnius prolixus* et *Rhodnius pictipes* vecteurs naturels de choix de *S. cruzi* (Study of *Trypanosoma cruzi* Infection in French Guiana.) Institut Pasteur de la Guyane et du Territoire de l'Inini Publication No 117 1945 Nov 5 pp

Triatomidae captured in French Guiana belong to one or other of the following species: *Rhodnius prolixus*, *R. pictipes*, *Triatoma rubrofasciata*, *Parstrongylus gemiculatus* and *Eratyrus mucronatus*. LAROUSSÉ has recorded *R. robustus* also but the authors have not met with it. They have found trypanosome infection in *T. rubrofasciata*, *R. prolixus* and *R. pictipes* but in the case of the first they could not obtain the blood forms and animal inoculations in the laboratory remained negative and on one occasion only was xenodiagnosis positive. They think therefore that the trypanosome present in this insect is more often than common in bats not the human type of *T. cruzi*. Of four specimens of *R. pictipes* three were infected this has not before been noted as infected in nature. Further examination has shown that of 72 *R. pictipes* examined 65 were positive of *R. prolixus* 68 out of 80 but only 29 out of 91 *T. rubrofasciata*. The two former are therefore to be regarded as the natural vectors in French Guiana, *T. rubrofasciata* less commonly. The authors conclude. The experimental xenodiagnostic test seems to us to be of much value in determining what are the natural vectors of choice of *S. cruzi* in any given district. H Harold Scott.

BRASIL, A. Forma cardíaca crônica da Doença de Chagas. [Chronic Cardiac Lesions in Chagas's Disease.] Hospital Rio de Janeiro. 1946 Feb., v 29 No 2, 199–224 23 figs. [17 refs.] English summary

In August 1941 a Congress lasting for a week was held in Belo Horizonte in honour of Carlos Chagas. This is one of the papers read at that Congress. It is a concise but comprehensive account of the cardiac complications of this disease, dealing with the symptoms, diagnosis, prognosis and treatment and illustrated by 89 electrocardiographic tracings. Diagnosis is stressed between

this and arterio-sclerosis syphilis rheumatic carditis diphtheria congenital heart disease among other conditions. The whole is a very readable summary but there is nothing fresh and it does not lend itself to abstract. Those wishing to renew their knowledge of the subject would do well to read the English summary which is fairly full and contains all the important points of the original.

H Harold Scott

RAMOS J Jr & LAUS F J A. Miocardite crônica na tripanosomíase americana. Considerações clínicas em torno de seis casos [Chronic Myocarditis in American Trypanosomiasis. Discussion of Six Cases.] *Hospital Rio de Janeiro* 1946 Feb v 29 No. 2 231-50 14 figs English summary

Evidence has been accumulating in recent years to show that sufferers from non valvular disease of the heart often owe their condition to *T. cruzi* infection. The present communication deals with six patients 5 men and 1 woman their ages ranging from 29 to 66 years. The dates of infection could not be determined in four in the other two it was 10 and 15 years previously but all had lived in *Triatoma*-infested localities. Their symptoms were mainly dyspnoea and epigastric pain on exertion and marked debility with palpitation and headache giddiness and cough with mucoid sputum. None of these symptoms is of course characteristic of Chagas's disease they are common to myocarditis of any origin but electrocardiograms show that the lesion is in this disease situated in the Bundle of His or in the sinoauricular node [we must remember that the conclusions are here based on a very small number of cases] with resultant arrhythmia and signs of heart-block. Of the six cases detailed three ended fatally with the usual signs of cardiac failure. The others improved in that oedema cleared up the dyspnoea became less troublesome and the heart diminished in size. These three were diagnosed, one by a positive xenodiagnostic test the other two by positive Guerreiro-Machado reactions. The three fatal cases had given negative results to xenodiagnosis but the Guerreiro-Machado test could not be carried out owing to temporary lack of antigen. Diagnosis in them was made by post-mortem findings. The moral to be drawn from this is that *T. cruzi* infection should be suspected and looked for in all patients with myocardial lesions who live in or have come from regions where the vectors prevail.

H Harold Scott

MAZZA, S BASSO G & BASSO R. Investigaciones sobre enfermedad de Chagas. Esquizontipánides ulcerosas tardías en enfermedad de Chagas y otras manifestaciones eruptivas. [Studies in Chagas's Disease Late Ulceration and other Outaneous Manifestations.] *Universidad Buenos Aires Misión de Estudios de Patología Regional Argentina (Jujuy)* Publicacion No 71 1946 42 pp. 32 figs

Several eruptions may be seen in patients infected by *T. cruzi* urticarial erythemas morbilliform rashes have been described but the present article illustrates other forms perhaps rarer certainly more distinct. Small, punched out ulcers may be seen on the foot lip and elsewhere. A good illustration shows the differences between these and the punched-out ulcer of American leishmaniasis. Crusted healing ulcers of the lips and face and papular eruptions of the face and neck are not uncommon another photograph shows a dense papular eruption of the thigh yet another a child with extensive impetigo-like lesions of the chin neck and chest. These lesions usually heal well under treatment with 7602 (Ac) Bayer but leave pigmented scars.

H Harold Scott.

DE FREITAS J. L. P. Inquérito preliminar sobre moléstia de Chagas no Município de Cajurú Estado de São Paulo Brasil. (Preliminary Investigation of Chagas's Disease in Cajurú, Brazil.) *Hospital* Rio de Janeiro. 1946 Feb. v 29 No 2, 155-65 10 refs English summary

## FEVERS OF THE TYPHUS GROUP

TORTING N. H. & SHEPARD C. C. The Preparation of Antigens from Yolk Sacs Infected with *Rickettsiae*. *Pub Health Rep* Wash. 1946 May 17 v 61 No 20 701-7 1 fig 11 refs

Three methods of preparing antigen from yolk sacs infected with *Rickettsia prowazekii*, *R. mooseri*, *R. rickettsii*, *R. barnesi* and *R. orientalis* are described. It was found that no single method was satisfactory for all these species of rickettsiae. All the methods were modifications of Craigie's diethyl-ether method. The antigenic potency of the products was estimated by complement-fixation tests applied to the sera of guinea-pigs which had been unimmunized by homologous strains of rickettsiae. In all three methods homogenized yolk sac cultures were used. In Method 1 a 10 per cent suspension was shaken directly with one-and-a-half volumes of ether. In Method 2, a 10 per cent suspension was centrifuged to sediment the rickettsiae before treatment with ether and the rickettsiae were resuspended in one-tenth of the original volume of saline so there was a ten-fold concentration. In both of these methods when *R. prowazekii* and *R. mooseri* were dealt with, the final product contained large quantities of antigen released by the ether and contained in the supernatant fluid after centrifugation. With *R. rickettsii* much less of this soluble antigen was released, with *R. barnesi* and *R. orientalis* there was no release at all but rather a loss of antigen. The methods therefore were quite unsuitable for the preparation of *R. orientalis* antigen.

In Method 3 the homogenized yolk sacs were shaken with 10 volumes of ether at a temperature of 4°C for 30-60 minutes. After standing for a short time the ether became yellow and a reddish mass of tissue fell to the bottom. The ether was decanted and fresh ether was added once or twice till it ceased to become yellow. After final decanting, about 1.0 cc. of distilled water was added for each gramme of yolk sac and after shaking the ether still in solution was removed under a partial vacuum. The suspension was kept overnight in a refrigerator and then centrifuged. The antigens were contained in the clear-red supernatant. In the case of *R. orientalis* the sediment also contained a considerable amount of antigen. By this method a satisfactory antigen was obtained from yolk sacs infected with *R. orientalis* the complement fixation titre was 1-128 as compared with one of 1-8 for the original crude 10 per cent suspension and titres of 1-2 for the preparations made by Methods 1 and 2. With *R. barnesi* there was actually a loss of antigen when Method 3 or any other method of ether extraction, was used. With *R. rickettsii*, *R. prowazekii* and *R. mooseri* Method 3 gave much the same results as the other two methods. The titre with *R. rickettsii* was 1-32, with the other two organisms it was in excess of 1-2,048.

The authors state quite clearly that no demonstrable immunization has been produced in mice inoculated subcutaneously with any antigens prepared from yolk sacs infected with tsutsugamushi disease. *John H. D. Meyer*

TOPPING N H & SHEPARD C C A Method for the Preparation of Tsutsugamushi (Scrub Typhus) Antigen from Infected Yolk Sacs. *Pub Health Rep Wash.* 1946 May 31 v 61 No 22 778-81

This paper by the same authors as the one reviewed above was scheduled for publication on March 2 1945 but was withheld because of the subject matter. The method described has presumably been superseded by Method 3 dealt with in the preceding abstract but the paper will be of historical interest to all workers on the preparation of rickettsial vaccines.

John W D Megaw

CHALKE H D Typhus Experiences in the Central Mediterranean Force  
*Brit Med J* 1946 June 29 977-80 July 6 5-8 1 chart & 1 fig

The author tells how the allied forces succeeded in keeping remarkably free from typhus fever during military operations in North Africa Italy and Yugoslavia in spite of the great prevalence of the disease among the people of these countries and in spite of the fact that none of the hygiene staff officers were informed of the projected landing in North Africa till the forces had actually embarked.

The preparations for dealing with the disease among the British troops consisted in the provision of large quantities of the powder A.L.63 (which contained derris and naphthalene) and of large numbers of portable disinfectors. Medical staff-officers were inoculated with a Cox type vaccine and talks were given before landing to officers and men.

After landing contact was made with the French Chief Officer of Public Health of Algeria who stated that between October 1941 and September 1942 nearly 40 000 cases of typhus fever had been reported and that he believed the real incidence to have been at least six times as high as this. One important safeguard was the fact that hardly any cases occurred in the large towns in which the people had been vaccinated by Blanc's liver marine vaccine. About two million persons had received this vaccine by the end of 1942. The killed vaccine of Durand and Giroud was used for doctors and others exposed to special risks and although there were many cases of typhus among the 71 000 persons who received the vaccine no deaths were known to have occurred. All the American troops had been vaccinated before landing but for the first few months the British troops were not protected in this way and they had to rely on regular hand-dusting with A.L.63 and on intensive propaganda. In 1943 there were about 34 cases of louse borne typhus and six of other forms of typhus among the British forces. When native-labour forces were enlisted, the recruits were bathed, disinfested, and inoculated with the Blanc vaccine.

The author tells the story of the much publicized epidemic in Naples. The city was occupied by the Fifth Army in October 1943. In November there were rumours that typhus was occurring and on investigation it appeared that the reports were well-founded. A conference of British and American hygiene officers was at once called this was attended by Italian public health doctors. A representative committee was set up a meeting of the medical men of Naples was held and prompt action was taken to search for cases and to disinfest all hospital patients and contacts.

From November 16 the incidence in successive weeks was —18 18 22, 45 and 36 cases then a sudden rise occurred in the week December 22 to 28 with 138 cases.

Early in December Dr Soper and Dr Davis of the Rockefeller Foundation arrived and by the middle of the month systematic case searching and widespread disinfestation of contacts with the American powder MYL (containing

pyrethrum) were in operation. An important point was the initiation of the system of disinfection by applying the powder with dust guns without removing the clothing by this method large numbers of persons could be disinfested as many as 60 000 were dealt with daily and by the end of February 1944 2,250 000 dustings had been carried out.

The U.S.A. Typhus Commission team arrived in December and began work early in January 1944. Details of the very thorough system of control established under the direction of the Commission have already been fully reported. The operations were unprecedented, both in their magnitude and in the completeness of the organization. Large quantities of 10 per cent. DDT powder became available early in January.

The author states that the measures adopted up to December 23 had already brought the epidemic under control because after the week ending January 11 there was a sudden fall from 340 to about 170 in the weekly number of cases reported. He assumes a time lag of about 18 days made up of the 12-day average incubation period and the average delay of six days in reporting the cases. This view will not be universally accepted. There were still as many as 130 cases in the week ending February 8 and in the following week there was a sharp drop to 40 cases so that allowing for the same time lag it may be argued that control became really effective towards the end of January.]

The conditions prevailing in Naples at the time of the epidemic are described in vivid language. They were such that a devastating epidemic would have been expected to occur during the first half of 1944 whereas the disease had disappeared from the city by the middle of April.

The remarkable results obtained are attributed to the perfection of the methods adopted and to the close and amicable co-operation between the British and American medical officers, the U.S.A. Typhus Commission, the Rockefeller Foundation team, the Allied Commission, the Allied Military Government, the Italian civil and military doctors, and the troops themselves.

The British troops and their attached civilian workers were protected only by MYL or A.L. 63 powder. Few of them were inoculated, yet only two or three cases occurred in this large group. The only British soldier attacked was a deserter who was heavily infested with lice. *John W. D. Alagar*

ZARAFONETIS C. J. D. ECKE R. S. YEOHANS A. MURRAY E. S. & SNYDER J. C. Serologic Studies in Typhus-Vaccinated Individuals. III. Weil-Felix and Complement Fixation Findings in Epidemic Typhus Fever occurring in the Vaccinated. *J. Immunology* 1946 May, v. 53 No. 1 15-30 [17 refs.]

The authors working with the U.S.A. Typhus Commission in Cairo have studied the Weil-Felix and complement-fixation reactions occurring at various stages of attacks of typhus fever in patients who had been protected by an epidemic typhus vaccine of the Cox type. Of the 31 cases investigated 29 were diagnosed with certainty or with a high degree of probability as epidemic typhus; the other two were cases of murine typhus contracted in West Africa. The conclusion was reached that the reactions can safely be used to establish a laboratory diagnosis of typhus fever in vaccinated persons provided that allowance is made for the higher degree of cross-fixation for epidemic and murine typhus that occurs among these persons as compared with unvaccinated patients. The paper is complementary to one by PLOTZ and WEITMAN who carried out similar tests on murine-typhus patients previously vaccinated with epidemic typhus vaccine. See this *Bulletin* 1946 v. 43 429.]

In all the 31 patients the rises observed in the titres of the Weil-Felix (O & I) and complement fixation reactions were higher than had ever been observed by the authors among healthy persons who had received "booster" doses of

the vaccine or among vaccinated persons who were suffering from other febrile diseases. In two of the 29 cases of epidemic typhus the murine-complement fixation titre reached the same high level as the epidemic titre but in most of the other cases the epidemic titre was four or more times as high as the murine.

Strangely enough the two patients diagnosed as having murine typhus had epidemic titres rising to 1-512 and 1-1 024 whereas their murine titre was only 1-256 in each case.

The authors suggest that the high degree of cross-fixation observed among vaccinated patients may be due to the presence of a common antibody produced in the serum in response to the action of the antigen common to epidemic and murine rickettsiae that is contained in the vaccine the common antibody would be expected to fix complement in the presence of antigens either of the epidemic or murine type.

Two of the patients suffered from laboratory infections the serum of one of these had given an epidemic typhus complement fixation reaction at a titre of 1-8 about two months before the onset and also on the second, third and fourth days of the illness the titre rose to 1-32 on the fifth day this patient's serum was known to have contained a considerable amount of neutralizing antibodies two months before the illness as shown by tests with gerbils so that the immunity known to exist beforehand had obviously not been enough to prevent infection but only to modify the severity of the attack.

John W D McGraw

SHEPARD C C & WICKOFF R W G The Nature of the Soluble Antigen from Typhus Rickettsiae. *Pub Health Rep Wash.* 1946 May 31 \ 61 No 22 761-7 8 figs on 4 pls

With the help of the electron microscope the authors have investigated the physical characteristics of the filter passing soluble antigen which is liberated from suspensions of epidemic and murine rickettsiae by ether treatment. This antigen has now been shown to consist of sub-microscopic particles of a capsular substance which adheres to and partly envelops the rickettsiae contained in a suspension purified by centrifugation. The term droplets is also applied to the particles which, though not uniform in size are so small that most of them could pass through bacterial filters. A photograph at a magnification of 18 000 diameters shows clearly a large number of the rounded particles present in a film prepared by evaporating a minute drop of the supernatant fluid obtained by high speed centrifugation of warm-ether extracts of homogenized yolk sacs infected with murine rickettsiae. The dried films were "shadowed" by coating them with an obliquely deposited film of gold by the method of WILLIAMS and WICKOFF (*J of Applied Physics* 1946 \ 17 23).

Seven other photographs prepared on the same lines show (1) *R. prowazeki* and *R. mooseri* from untreated suspensions (2) *R. prowazeki* after extraction with ether and demonstrating that the liberation of the particles from the capsular substance is much more active and complete with warm-ether treatment than with cold-ether treatment and (3) clumps of particles of soluble murine antigen agglutinated by homologous immune serum of rabbits.

John W D McGraw

GIROUD P Démonstration faite au sujet des corps homogènes inclusions du typhus exanthématique [Demonstration of the Homogeneous Inclusion Bodies of Exanthematic Typhus.] *Bull Soc. Path Exot* 1946 \ 39 Nos. 3/4 83-6.

The author describes the results of further investigation into the various forms assumed by the rickettsiae of typhus fever and the products of their action on the invaded cells.

The bodies now described were obtained from animals whose initial resistance to infection was being broken down. Smears containing the bodies were fixed treated with acetone and stained by Giemsa's method.

Side by side with blue-staining homogeneous bodies other intracellular purple ('aubergine-coloured') rounded bodies of similar size were seen on the surface of the latter there were one or more small masses of about one  $\mu$  in diameter which gradually became transparent lost their central portion and assumed the form of rings with one or more thickenings. At a later stage each ring broke into two or three parts, each of which at first consisted of a slightly curved rickettsia with pointed ends and later became like a normal bacilliform rickettsia.

Another transformation of blue-stained homogeneous bodies was sometimes seen in which they became broken up into transparent elements of three to four  $\mu$  in diameter each containing an unstained vacuole which later showed a chromatin-stained particle in its centre. Sometimes each element contained three or four vacuoles of the same kind. Soon the appearance of the original homogeneous body became changed to one of an enlarging granular body resembling a compact swarm of bees.

The author regards the homogeneous bodies as analogous with bacterial spores and as being capable of giving rise to bacilliform rickettsiae in the ways described.

(For the earlier studies on this subject by the author and PANTHER, see this Bulletin 1943 v 40 764 and 1942, v 39 733.)

John W D Meigs

CRAIGIE J WATSON D W., CLARK Emma M. & MALCOMSON M. Elizabeth.  
The Serological Relationships of the Rickettsiae of Epidemic and Murine Typhus. *Canadian J. Res. Sect. E. Med. Sci.* 1946 Apr v 24 No 2 84-103 5 figs. (17 refs.)

This paper was submitted as a confidential document in September 1943. Breinl and Madrid strains of epidemic rickettsiae and the Castañeda strain of murine rickettsiae were used in the experiments which are described in detail by the authors.

Specific differences were shown to exist between the complement fixing antibodies of epidemic and murine rickettsiae by removing the antibody common to both types from immune sera by the addition of rickettsiae of the heterologous types. Sera treated in this way were tested by the complement-fixation reaction and gave much higher titres with the homologous than with the heterologous antigen.

The type-specific complement-fixing antigen was found to be inactivated by heating for one hour at a temperature between 56° and 65°C. and so was shown to be thermolabile the thermostable antigen remaining after this treatment was found to be the same for both types of rickettsiae.

The Giroud rabbit skin reaction was found capable of being applied to differentiate between the specific heat labile antigens of epidemic and murine rickettsiae.

Small doses of murine or epidemic vaccines immunized mice against the toxic factors of homologous but not of heterologous rickettsiae when these vaccines were heated to 56°C. for 45 minutes much larger doses were needed to immunize the mice and the resulting immunity was the same for heterologous as for homologous toxins.

From the above and other experiments it appeared that epidemic and murine rickettsiae contained a common thermostable antigen and that each of the two types of rickettsiae contained a type-specific thermolabile antigen.

The authors state that there seems to be full justification for the suggestion made by Felix that there is an analogy between the heat-labile and heat stable antigens of rickettsiae on the one hand and the Vi and O antigens of the typhoid bacillus on the other.

No claim is made that the findings described necessarily apply to every strain of the two types of rickettsiae the authors refer to the need for an antigenic analysis of intermediate strains.

Full details of these important experiments will be found in the paper

JOHNSON Mary B & DAMON S R The Serologic Diagnosis of Endemic Typhus III. The Incidence and Titer of Complement-Fixing Antibodies in Random Samples of the Population in Endemic and Nonendemic Typhus Areas. *J Lab & Clin Med* 1948 May v 31 No 5 550-51

Complement fixation tests were carried out for endemic typhus [presumably the murine type] on the sera of —(a) 500 persons who formed a random sample of the population of Houston County in southern Alabama where the disease is endemic and (b) 400 corresponding persons from Morgan County in northern Alabama where the disease is rare.

In the former group there were 58 reactions at titres of 1-4 or over in the latter there was only one positive reaction. The titres observed were 1-4 to 1-16 in 41 of the 59 positive sera and 1-32 to 1-256 in the remaining 18.

The authors point out that these findings have an important bearing on the significance of the reaction as a diagnostic test for febrile diseases occurring in areas where endemic typhus is prevalent.

LE CHUTTON F & BERGE C A propos de la présence d'agglutinines anti Eberth para A ou para B dans le sérum de sujets vaccinés au T.A.B. atténués de typhus murin nautique [The Presence of Typhoid and Paratyphoid Agglutinins in the Sera of Murine-Nautical-Typhus Patients who had been Vaccinated with T.A.B. Vaccine] *Bull Soc Path Exot* 1946 v 39 Nos. 3/4 103-10

Details are given of the results of repeated Widal and Weil-Felix tests carried out on 11 patients suffering from murine nautical typhus. Four patients taken at random were examined, and only three developed no agglutinins for typhoid or paratyphoid bacilli during the course of the attack.

In one group of seven cases the typhoid titre reached a maximum ranging from 1-80 to 1-10,240 and although the Weil-Felix titre was considerably higher in five of these it was the same (1-2,560) in one and lower (1-120 against 1-10,240) in another.

In another group consisting of two cases the titres with both typhoid and para A bacilli rose to 1-320 or over in one of these the typhoid titre reached 1-40,000 the para A titre 1-320 and the Weil-Felix titre 1-1,280 all on the 10th day in the other the corresponding titres were 1-320 1-640 and 1-320. In the latest group, which also consisted of two cases the para B titres reached 1-160 and 1-320 respectively and the Weil-Felix titres were 1-640 and 1-10,240.

The diagnosis of murine typhus was regarded as certain in all the cases of the series blood cultures were sterile in every one and in several of them rickettsiae were isolated by guinea pig inoculation.

The author points out that the sera of typhus patients are well known to have an increased power of agglutinating numerous kinds of bacteria and that in febrile patients who have been inoculated with T.A.B. vaccine the Widal test is of little value in diagnosis.

John W D Megaw



LE GAC P. Etude sur le typhus tropical des savanes de la haute Côte d'Ivoire.  
[A Study of Tropical Typhus in the Savannas of the Upper Ivory Coast.] *Bull Soc Path Exot* 1946 v 39 Nos. 3/4 86-94

Since December 1941 the author has studied the seasonal outbreaks of "grippe" which occur in the Upper Ivory Coast in close association with the seasonal trapping or burning out of wild rodents by the indigenous population who greatly relish these animals as an article of diet. Certain tribes in the area regard the red rat (*Mus rufinus*) as responsible for the outbreaks of the disease and forbid the eating of its flesh. Several Europeans who have entered the affected areas or have come into contact with rats driven out by the prairie fires are known to have been attacked by the disease.

Louse transmission is regarded as unlikely on epidemiological and serological grounds. The occurrence of definite outbreaks and the absence of local sores are considered to be improbable in a tick borne disease and larval mites have not been found in the African savannas. For these reasons the author believes that the rat flea *Xenopsylla cheopis* is the most likely vector though he also argues that the infection probably enters the body through the mucosae especially by ingestion of food contaminated by the hands of the rat hunters or by the urine and faeces of infected rats.

Twenty-two cases of which one was fatal, were seen among Europeans. The rash is said to have been much less conspicuous than that of louse borne typhus and to have differed from the rash of the tick-borne disease in being restricted to the chest. The intradermal hypersensitivity test with formalized vaccine supplied by Durand and Giroud (presumably of the epidemic typhus type) was positive in 14 of the 16 patients tested during convalescence. The Weil-Felix responses were varied. From the tables it appears that the following reactions at titres of 1-100 or over were observed in 31 tests. With *Proteus* OX19 16 were positive (1-100 to 1-200) and of these 12 were positive also with *Pr* OXA. With *Pr* OXA 13 were positive (1-100 to 1-500) and 12 of these were positive also with *Pr* OX19. With *Pr* OX2 all were negative at 1-100 and only two reacted at 1-50.

No significant reactions were observed among Patas monkeys, guinea-pigs or rabbits inoculated by the intraperitoneal route and passage inoculations from these animals were negative even among rats. Sera of inoculated monkeys and rabbits agglutinated *Pr* OX19 at titres of 1-50 to 1-150 and *Pr* OXA at 1-20 to 1-150.

The author states that "the specific *Proteus* of the disease has not yet been demonstrated, but that the epidemiology, symptomatology and serum reactions suggest that the fever belongs to the group of tropical typhus fevers (type scrub typhus of Malaya).

[See the comment on the following paper by the same author.]

John W. D. McGeen

LE GAC P. Recherches sur les typhus des savanes de l'Ouhangoua - Applied to the disease des Bougbons. [Heat-labile antigens of epidemic and murine, Chari Savannas.]

1946 v 39. Murine or epidemic vaccines immunized mice against

The author found that 56°C. for 45 minutes much larger dose research into the Typhus Fever of the Chari was similar in the resulting immunity was the Disease of the Bougbons? Bull Soc Path and the pericardial above and other experiments. 44 87 100. with *Yersinia* contained a common th but very is of rickettsiae contained cells with investigations carried out in 1938 into a form of rickettsiae and clinical features of the disease of which was in French Equatorial

Guinea-pigs inoculated with the blood of infected persons had a febrile reaction lasting four or five days after an incubation period of about ten days but there was no scrotal reaction

The fever is said to correspond in severity to louse-borne typhus and it is estimated that 2 000 to 3 000 persons die yearly in the area between the Cameroon border and the Anglo-Egyptian Sudan

[The special interest of this and the preceding paper is that they contain evidence of the widespread occurrence in tropical Africa of a fever of the typhus group which appears to be primarily a disease of animals of the wilds. Although much of the evidence points strongly to flea transmission the serological and experimental findings are not such as would be expected in flea borne typhus. The author's suggestion that the disease should be classified as tropical typhus is not happy but there will be general agreement with the other suggestion that more research is needed to solve the problem of the transmitting vector.]

John W. D. Megaw

LE GAC P. Réaction d'hypersensibilité à l'injection intradermique de rickettsies tuées chez des sujets ayant présenté un typhus tropical [Hypersensitivity to Intradermal Injection of Killed Rickettsiae in Patients with Tropical Typhus.] *Bull Soc Path Exot* 1946 v 39 Nos 3 4 95-7 1 chart.

MACKIE T T DAVIS G E. FULLER H S KNAPP J A STEINACKER M L. STAGER K E. TRAUB R. JELLISON W L MILLSPAUGH D D AUSTRIAN R. C. BELL, E J KOHLIS G M WEI HSI & GIRSHAM J A. V. Observations on Tsutsugamushi Disease (Scrub Typhus) in Assam and Burma. Preliminary Report. *Amer J Hyg* 1946 May v 43 No 3 195-218 4 figs (1 map) [21 refs]

This paper is a preliminary report by a team of 14 workers of the U.S.A. Typhus Commission into the epidemiological and other conditions connected with the occurrence of mite-borne typhus in the China Burma India theatre of war from December 1944 to November 1945. The workers acknowledge the great assistance received from American and British voluntary helpers.

Towards the end of 1943 the disease was recognized as a serious military problem for the troops engaged in exercises and operations on the Assam Burma frontier and in Burma. From early November 1943 till early September 1945 there were 1 088 cases among American and Chinese troops with a case-fatality rate of 8.9 per cent. There were five peaks of incidence these at first suggested that there was a pronounced seasonal rise in spring and autumn but they were found to correspond with periods of combat and with training operations in special areas. For example in January 1945 there were 65 000 U.S.A. troops in Assam and Burma, yet of the 194 cases in that month all but nine occurred among 6 000 troops engaged in combat.

Certain outbreaks among Chinese troops appeared to be associated with the habit of bathing in a river on whose grassy banks the soldiers spread out their 10th ~~was~~ dry, and in one such locality the grassy ground was found heavily

In the latest group winter also consists by the Chinese troops was also reached 1-160 and 1-320 respectively and the well road from Ledo in

The diagnosis of murine typhus was regarded as certain 13 genera of the series blood cultures were sterile in every one and in 45 new rickettsiae were isolated by guinea-pig inoculation.

The author points out that the sera of typhus patients are weakly agglutinated by a small number of kinds of bacteria. In patients have an increased power of agglutinating numerous kinds of bacteria. In febrile patients who have been inoculated with T.A.B. vaccine the test is of little value in diagnosis.

John W. D.

*flavipectus yunnanensis* and (4) 4 from the tree shrew *Tupaia belangeri* *retzius*. Three strains were isolated from laboratory white rats, and one from the pooled tissues of 4 gerbils which had been experimentally exposed to mite attacks in endemic regions. The preponderating mite was *Trombicula deliensis* which was the only mite found in 24 of the pools from which infection was isolated and which was present in every one of the positive pools.

Transovarial transmission of *R. orientalis* was demonstrated by hatching, in the laboratory, eggs of *T. deliensis* from infected localities and causing the larvae to feed on susceptible animals.

Incompletely engorged mites sometimes became detached from the initial host and afterwards completed their meal on another animal. In four experiments with *T. deliensis* the reattached larvae caused infection in laboratory animals.

The rat and tree shrew already mentioned were the only mammals found naturally infected though three strains were recovered from mites obtained from Sladen's roof rat (*Rattus rattus sladeni*). A complete investigation of the numerous animal hosts of *T. deliensis* was impracticable.

In the three areas along the Stilwell Road in which hyperendemicity was indicated by exceptionally high attack rates among troops *T. deliensis* constituted 60.74 and 98 per cent respectively of all the mites collected; a high incidence of this mite therefore indicates that the area should be strongly suspected. There was also evidence that areas in which cases of the disease have occurred remain risky for at least one year. John W D Meyer

VAN DEN ENDE M LOCKET S HARGREAVES W H NIVEN J & LEWYHOFF  
L. Accidental Laboratory Infection with Tsutsugamushi Rickettsia.  
*Lancet* 1946 July 6 4-7 4 charts.

In spite of the strictest precautions four persons became infected with tsutsugamushi disease in the course of work connected with the large-scale production of vaccine made from the lungs of cotton rats [see this *Bulletin* 1946 v 43 435 and 436]. All the patients had been protected by Fulton and Joyner vaccine of the cotton-rat lung type. The duration of the fever was 14-16 days in three of the cases and at least 19 days in the fourth. One of the patients became "critically ill on the sixth day" when she had a faint heliotrope cyanosis; another was very ill on admission and thereafter her mental and physical condition deteriorated till she became unable to take fluid by the mouth. The other two patients do not seem to have been dangerously ill at any stage of the disease. All the patients made good recoveries, and the authors conclude that as there were three deaths among five previous patients known to have had laboratory infections with *Rickettsia orientalis* the vaccine may have had significant value in protecting against death.

From the details supplied of the clinical features of the attacks it appears that these conformed with those often observed in the naturally acquired disease. Delirium was severe in one case and mild or very slight in the others. In three cases there was a local lesion at the site of infection [see subangul-]. In two of these there was an associated local adenitis. Numerous *Exot* repeated falls of the temperature were features of two cases; in the fever curve was of the continued type.

The Weil-Felix (OAK) reaction was positive in every case to a fever which maximum titre was only 1-160; this was reached on the day the disease described *orientalis* was isolated from the blood taken on the day the Equatorial Africa peritoneal inoculation of mice and guinea-pigs. In the rats which swarmed were isolated from blood taken on the sixth day; contained numerous fleas

Infection of the different patients occurred in the following ways—(1) From a prolonged bite by a cotton rat which had just received intranasal inoculation the incubation period was 14 days (2) Probably by droplet infection occurring in the course of work which involved the transfer of virulent lung suspension by a Pasteur pipette from centrifuge tubes to ampoules. By actual test it was found that bubbling with the discharge of droplets into the air was almost unavoidable during this procedure (3) By a puncture of the skin through a rubber glove with an accidentally broken pipette which had just been emptied of a virulent suspension of the rickettsiae. A tourniquet was applied within half a minute the wound was excised within five minutes bleeding was encouraged and antiseptics applied. An injection of 1.0 cc. of vaccine was given at once and on the same day 10 cc. of phenolized serum from an immunized rabbit was injected. On the next day 12 cc. of phenolized serum from a patient in the third week of convalescence was injected intramuscularly. The incubation period was 11 days (4) Through washing by hand Petri dishes which had contained infected cotton-rat lungs. This action was in gross contravention of the rules so the patient did not report the occurrence. The incubation period was about 17 days according to the statement made later by the patient  
John W. D. Megaw

SMADEN, J. E., RIGHTS, F. L. & JACKSON, Elizabeth B. Studies on Scrub Typhus. II. Preparation of Formalinized Vaccines from Tissues of Infected Mice and Rats. *Proc Soc Exper Biol & Med* 1946 Mar; 61 No 3 308-13 1 fig

The authors mention the interesting fact that after a number of unsuccessful attempts to produce a potent inactive vaccine against scrub typhus three promising methods have been reported almost simultaneously. These were as follows in brackets are the dates of the original confidential reports in which they were first described—(1) FULTON and JOYNER's rodent-lung vaccine (June 21 1944) [see this *Bulletin* 1946; 43 435] (2) A tissue-culture vaccine of PLITZ and his co-workers (September 23 1944) [see the abstract immediately following this] and (3) A rodent tissue vaccine (October 2, 1944) as described in the present paper.

White mice white rats or cotton rats were inoculated intravenously with suspensions of infected yolk sacs the estimated dosage was  $10^4$  M.L.D. of *R. orientalis*. On the 4th or 5th day the animals were moribund or dead their lungs and spleens were homogenized and a 10 per cent suspension in normal saline was prepared and freed from large particles by centrifugation. Formaldehyde (0.1 per cent) and merthiolate (0.01 per cent.) were added and the suspension was stored at 5 C for 1-6 weeks. The strength in complement-fixing antigen was titrated, though it is stated later that the potency of the vaccine could not be estimated by this procedure.

Groups of 24-70 mice were inoculated intraperitoneally with three doses of 0.5 cc. of the vaccine at five-day intervals. After two weeks the mice were challenged with varied doses of homologous rickettsiae. Large numbers of mice had to be used because of the wide range of individual susceptibility of the animals. Details are given of the results of the tests and of the standards used in estimating the degree of immunity produced by the vaccine. *R. orientalis* was used in preparing white-rat vaccine till it was found that the area mapable of growth in a highly infective condition in yolk sacs. The northern strain of yolk-sac suspensions was easily estimated by observing the death of white mice injected intravenously with 0.5 cc. of a suspension. White rats were used for the preparation of the vaccine species were found large yield obtainable from each animal this amounted to 100 cc. The following strains of *Gerrillus gerbillus* (2) 53 from pooled suspensions

The authors regard their method as being preferable to the cotton-raf-lung method because bacterial sterility was not a problem intravenous injection is safe and simple and white rats are easier to obtain and handle than cotton rats.

The vaccines obtained by the three methods mentioned above are said to be of comparable potency but all are regarded as being difficult to exploit on a large scale.

John W. D. Megaw

PLOTZ H. BENNETT B. L. & REAGAN R. L. Preparation of an Inactivated Tissue Culture Scrub Typhus Vaccine. *Proc. Soc. Exper. Biol. & Med.* 1946 Mar. v. 61 No. 3 313-17

Yolk-sac cultures of *Rickettsia orientalis* were obtained from peritoneal exudate of infected mice and used in the preparation of tissue cultures by the method of Zimmer Plotz and Enders. The early yolk-sac cultures were poor in rickettsiae but by selection and repeated passages a rich growth was eventually obtained and this was found suitable for the preparation of satisfactory tissue cultures which constituted the vaccine. Full details of the method are found in the paper.

Some of the vaccines were of low potency when this happened it was found that the culture flasks had not been adequately examined to ascertain their richness in rickettsiae. The most potent vaccines had an immunity index of 3.7 to 4.5 logs in other words they induced protection against from 5,000 to 32,000 M.L.D.s of *R. orientalis*.

In one series of experiments mice received "booster" doses of vaccine and the induced resistance was greatly increased for example up to 7,800 to 80,000 M.L.D.s. This and the other two vaccines referred to in the preceding paper were regarded as being of comparable potency but the immunity conferred on white mice by all three vaccines was obtained only by the use of intraperitoneal inoculations never by subcutaneous injections.

It is admitted that the large-scale preparation of vaccine by the tissue culture method "would present certain technical difficulties" but for the protection of selected personnel it has the advantage of being a relatively clean product.

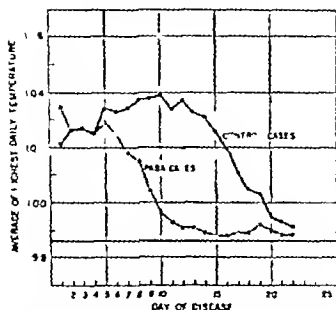
The yolk-sac method, which would be the most suitable for mass production has never been successfully prepared one reason being the deleterious effect of ether upon the antigen.

John W. D. Megaw

TIERNY N. A. Effect of Para Aminobenzoic Acid in Tsutsugamushi Disease. *J. Amer. Med. Ass.* 1946 May 25 v. 131 No. 4 280-85 2 charts. [10 refs.]

Strikingly good results were obtained from the administration of para-aminobenzoic acid (PABA) in the treatment of 18 scrub-typhus partly acquired American and Indian military hospitals at Ledo Assam. Therapeutic effect in these cases and almost without exception alternately admitted upon [see below] and in each hospital.

The chart shows that the average duration of the feases in the other two longer in the control group than in the treated. In three cases of the fever and symptoms occurred after the first day in one the this second spell of fever lasted three to 14 days ended on the fourth day and R. ill and no further doses of the drug were given on the second day by intra the general symptoms were pronounced ways. In another case the organisms became alert and the headache disappeared day.



Comparison of the average of the highest Fahrenheit temperature each day in 18 untreated control cases of scrub typhus and in 18 cases treated with para-aminobenzoic acid (PABA)

[Reproduced from the *Journal of the American Medical Association*.]

the treated had slight bronchitis whereas 14 of the controls had severe bronchitis. Full details are given in tabular form of the chief findings in the two groups of patients. The general results are shown in the following table —

*Severity of the Attacks among Treated and Controls*

	Mild	Moderate	Severe	Grave	Fatal
Indian treated (9)	8	1	0	0	0
American (8)	4	3	0	1	0
Chinese (1)	0	1	0	0	0
Total (18)	12	5	0	1	0
Controls (16)	1	1	4	7	3

The treatment was started on the 3rd day in four cases on the 4th day in five on the 5th day in three on the 6th day in four, and on the 7th day in two.

The drug was given by the mouth as a powder to each gramme of which 0.5 of a 5.0 per cent solution of bicarbonate of soda was added. The dosage challenged most effective was 8.0 gm. initially followed by 3.0 gm. every two hours. The total dose was 217-357 gm. for Indian and 217-513 gm. for American patients. Details of the drug in the blood was determined by the Marshall method as used for sulphanilamide [see *Science* 1938 July 22 85]. The area ml. of R. was 30-60 mgm. per 100 cc. but when the patients became anemic of growth was often reduced to 10-20 mgm. without recrudescence. The following table shows the average maximum concentration of white blood cells in the blood of patients was considerably higher (77 mgm.) than that of white blood cells in the blood of controls (56 mgm.) this difference suggests that the body of the patients was not have been sufficiently taken into account. Two (2) 53 from pooled suspension

of the Indian patients who had very high maximum concentrations of 152 and 155 mgm are said to have suffered from "confusion due to PABA" and the patient whose maximum concentration of 103 mgm. was the highest among the American group suffered from convulsions.]

There was a general tendency to leucopenia towards the end of the course of treatment—total counts of 4 000 per cmm or less were observed in nine of the treated and in only two of the controls. There was a satisfactory return of the leucocyte condition to normal in every case and the treatment was never curtailed because of leucopenia. It is recommended that the total white cell count should be determined every other day—if it falls below 4 000 a differential count should be made and if the granulocytes are less than 30 per cent. the drug should be discontinued. A total count of less than 3 000 is in itself a contraindication.

It is advised that when the blood concentration of the drug exceeds 60 mgm per 100 cc one dose should be omitted and the maintenance dose should be suitably reduced. The treatment should be started as early as possible but it may be worth trying even after the end of the first week. Sulphonamides are regarded as being contraindicated—bacterial complications should be treated with penicillin.

The diet of the treated and control patients was rich in proteins, calories and vitamins. 4.0 gm. of additional sodium chloride was given and the fluid intake was 3–4 litres daily.

In view of the results obtained in the present trials taken in conjunction with those reported by LEOWAKS and his co-workers in louse borne typhus [see this *Bulletin* 1945 v 42: 201] and the abundant evidence supplied by animal experiments the authors think it likely that PABA may prove to be a general anti-rickettsial drug.

John W D McGraw

ZARAFONETIS C J D, SVYDER, J C & MURRAY E S. Immunity following Para-Aminobenzoic Acid Therapy in Experimental Tsutsugamushi Disease (Scrub Typhus). *Proc Soc Exper Biol & Med* 1946 Mar v 61 No 3 240–42 [Refs. in footnotes]

Gerbils which had recovered from experimental infection with the rickettsiae of tsutsugamushi disease with the help of para-aminobenzoic acid (PABA) were tested six to nine months later and found immune to three different strains of *Rickettsia orientalis* administered by the intraperitoneal route in doses ranging from 2,140 to 31 600 lethal doses. There was only one death among the 69 gerbils used in the test. Ceylon, Calcutta and Karp strains of *R. orientalis* were used to infect different groups of the gerbils and the animals belonging to each group were divided into three subgroups, one of which was challenged by the homologous strain of rickettsiae and the others by heterologous strains. Complete immunity was found to exist irrespective of the strains used in the original infection and the immunity tests so that cross immunity had obviously been produced. The findings were regarded as showing that the action of PABA is to inhibit the growth of rather than to kill, the rickettsiae.

John W D McGraw

BUSHLAND R C. Tests against Chiggers in New Guinea to develop a Practical Field Method for Impregnating Uniforms with Dimethyl Phthalate for Scrub Typhus Prevention. *Amer J Hyg* 1946 May v 43 No. 3 219–29.

Trombiculid mites are a serious nuisance in many temperate and tropical regions as well as being the vectors of scrub typhus. Some protection may be obtained in many ways the most familiar being by dusting the socks and garments with sulphur but this is not reliable enough when dealing with scrub

typhus. Experiments were carried out in New Guinea using the larval mites *Trombicula buloensis* and *Schöngastia pusilla* which appear to be similar in their reactions to the actual vectors of scrub typhus (*T. fletcheri* and *T. walchi* have been incriminated) which cannot be obtained in sufficient numbers for experiments. [It will be remembered that PHILIP *et al* (this Bulletin 1946 v 43 733) regard *T. fletcheri* and *T. walchi* as synonyms of *T. akamushi* and *T. deliensis* respectively]

Garments were impregnated in bulk with an emulsion of 5 per cent dimethyl phthalate 2 per cent soap and water. This could be made up without any special apparatus and after drying it left about two ounces of dimethyl phthalate in each set of garments. This gave no discomfort except a slight burning sensation in the scrotum which was prevented by using untreated underpants.

The garments were tested by placing live mites on the material and measuring the stopping time i.e. the time taken to paralyse the mites. If this occurred in less than 15 minutes then the garment was considered protective. Volunteers also exposed themselves in areas where mites caused scrub itch but from which typhus was believed to be absent. Impregnation gave almost complete protection up to five weeks if the garments were not laundered and it withstood some rinsing in cold water but protection was lost after proper laundering or after long wading in fresh or salt water.

Kenneth Mellanby

BUSHLAND R. C. New Guinea Field Tests of Uniforms Impregnated with Miticides to develop Laundry-Resistant Clothing Treatments for preventing Scrub Typhus. *Amer J Hyg* 1946 May v 43 No 3 230-47

It has been shown (see BUSHLAND above) that uniforms impregnated with dimethyl phthalate give good protection against trombiculid mites but that this protection is lost after the garments are laundered. Other substances toxic to mites were tried and dibutyl phthalate and benzyl benzoate gave the best results. The benzyl benzoate impregnated from a soap-and-water emulsion at the rate of two ounces per fatigue uniform (jacket trousers socks) gave practically complete protection until the garments had been laundered three times at 210°F. Dibutyl phthalate was less effective at the outset but it withstood washing better. A mixture of equal parts of benzyl benzoate and dibutyl phthalate is advocated.

Kenneth Mellanby

HARRELL G. T. WOLFF W. A. VENNING W. L. & REINHART J. B. The Prevention and Control of Disturbances of Protein Metabolism in Rocky Mountain Spotted Fever. The Value of Forced Feedings of a High-Protein Diet and of the Administration of Specific Antiserum. *Southern Med J* 1946 July v 39 No 7 551-7 1 fig

Nine children suffering from Rocky Mountain spotted fever were treated with a diet containing about twice the amount of protein present in the standard hospital diet. When necessary supplementary feeds of high protein liquids were given by gavage so as to bring up the total quantity of protein to 4.0 gm per kilo of body weight.

The general condition of the patients was observed to be much better than that of eight patients previously treated on the usual dietary. Oedema was less and there was a gain in weight during the illness in nearly every case. The serum proteins were maintained at slightly higher levels and there was evidence that the body proteins were being depleted to a less degree.

John W. D. Megaw



GLASGOW R. D. & COLLINS D. L. Control of the American Dog Tick, a Vector of Rocky Mountain Spotted Fever. Preliminary Tests. *J. Econom. Entom.* 1946 Apr. v. 39 No. 2 235-40 2 figs.

In recent years tick-borne Rocky Mountain spotted fever has been troublesome in parts of South-eastern New York State. The vector is the American dog tick *Dermacentor variabilis*. The cases which have occurred are deterring people from using the recreational facilities which exist in this area and the public health authorities are anxious for control measures to be devised as quickly as possible. In 1945 preliminary work was done with several insecticides of which DDT, gamma-hexachlorocyclopentadiene, rotenone and nicotine appeared to be promising. Lethane 334 Special and Halowax (chlorinated naphthalenes) were less effective. Mixtures were also tried, and one promising formula was 0.25 to 0.5 per cent DDT plus 0.08 to 0.125 per cent pyrethrins. 2 quarts of this were used per acre. For application the insecticides were dissolved in fuel oil or diesel oil, and were atomized by a paint sprayer connected to a mechanical compressor. It was proposed to try sprays applied by aeroplanes and aerosol fogs from thermal generators, for making large scale treatments. More extensive work was planned for 1946. *J. R. BURTON*

IRONS J. V. TOPPING N. H. SHEPARD C. C. & COX, H. R. Outbreak of Q Fever in the United States. *Pub. Health Rep. Wash.* 1946 May 31 v. 61 No. 22, 784-5.

An outbreak of more than 40 cases in March 1946 with two deaths in stock yard men in Texas. Investigations suggest that cattle are involved in the human infections. Clinical and serological evidence is in favour of Q fever, high complement fixation titres to Q fever antigens being found in sera from convalescents and rickettsia-agglutination tests being positive. The illness varied from mild fever to severe pneumonia. *Charles Wilcocks*

## YELLOW FEVER.

GAST-GALVIS A. Viscerotomy en Colombia. [Viscerotomy in Colombia.] Reprinted from *Rev. Medica*. Bogotá. 1945 Sept. & Oct. Nos. 553-554 34 pp. 4 figs. 3 maps & 1 graph. [12 refs.] English summary.

The Colombia Viscerotomy Service was started in September 1934 and now there are 200 viscerotomy centres and the number of specimens taken has reached 22,000. When first started the object was to find, from examination of liver tissue, the prevalence of yellow fever, but the value of the procedure is not so restricted and in this article the author records the findings in other diseases also such as malaria, sickle-cell anaemia, cirrhosis, acute yellow atrophy, tumours, etc. Of the 22,000 specimens taken 7,302 were from children up to 4 years of age and 1,927 from those between 5 and 9 years; i.e. 9,229 (42 per cent. of the total) from those under 9 years. Among the specimens 352 showed the changes of yellow fever, over 90 per cent. of these were from males and 136 (38.6 per cent.) were in the third decade; only 7 were from females.

Of other diseases diagnosed from viscerotomy specimens there were 2,447 cases (11.1 per cent.) of malaria (i.e. malarial pigment was present) most coming from the Magdalena Valley. Forty-three men and 28 women showed signs of sickle-cell anaemia or the sickle cell trait. Pathological changes of acute or subacute yellow atrophy of the liver were found in 175 subjects. Most of these came from the Bananera Zone of Magdalena, the next highest being the

south-west of Antioquia. Tuberculosis was seen in 391 specimens 116 (29 per cent) of which were from children under the age of 5 years and 115 from persons over 40 years. Signs of cirrhosis were present in 404 that is less than 2 per cent and syphilitic changes in 10 only. Thirty five showed tumours—adeno-fibroma (1) metastatic adeno-carcinoma (16 male 7 female 9) and sarcoma (2). One case of visceral leishmaniasis was seen in Santander Department the first to be diagnosed in Colombia.

H Harold Scott

## DENGUE

DIAZ RIVERA R S A Bizarre Type of Seven Day Fever Clinically Indistinguishable from Dengue *Bol Asoc Med de Puerto Rico* 1946 Mar v 38 No 3 75-80 7 figs. on 2 pls

[A contradiction in terms is contained in the title of this paper. If the disease is indistinguishable from dengue it cannot well be called a bizarre type of seven-day fever.]

The only important respects in which the authors regard the disease as differing from dengue are the absence of leucopenia and bradycardia but the evidence in support of the existence of these differences is not convincing. The total leucocyte count is stated as ranging from 3 000 to 7 200 per cmm. and as the days of the disease on which the counts were made are not stated these figures are by no means inconsistent with the diagnosis of dengue. There may have been a fall in the count during the illness. The leucocyte picture in other respects is suggestive of dengue since a definite lymphocytosis was observed in every instance. It is also stated that in at least 26 of the 53 cases seen at San Juan, Puerto Rico there was a tendency towards bradycardia.

Some of the chief features of the disease were—a duration of six days with sudden onset accompanied by aches and pains and retrobulbar pain in every case. There were severe body pains in 70 per cent a rash conforming to one of the types seen in dengue in 53 per cent, a biphasic fever curve in 70 per cent, and lymphadenopathy in 27.6 per cent. of the cases. The termination was by crisis or rapid lysis. It is stated that the vector and the other conditions favourable to the transmission of dengue were present. In view of these observations and of the absence of any other explanation of the outbreak, it seems strange that there should have been any hesitation in regarding the disease as dengue.

It is also stated that Dr W H. Glines of the City Hospital, San Juan, claims that dengue has been occurring in the locality "since the early thirties."

John H D Megaw

BULL. U.S. ARMY MED DEPT 1946 July v 6 No 1 4-5 Effective Vaccine against Dengue Fever

In this short note it is stated that an effective vaccine against dengue has been obtained from a strain of the virus isolated in Hawaii. This strain has undergone 32 passages through the brains of mice and has lost its power to provoke but not to prevent typical dengue.

Charles Wilcocks.

POLLARD M LIVESAY H R, WILSON D J & WOODLAND J C. Immunological Studies of Dengue Fever and Colorado Tick Fever *Proc Soc. Exper Biol & Med* 1946 Apr v 61 No 4 396-8 2 figs.

The authors have obtained experimental evidence which suggests that there is no immunological relationship between the agents of Colorado tick fever

and dengue fever. Their findings confirm those already reported by FLORE and his colleagues [this *Bulletin* 1946 v 43 737].

Two volunteers were inoculated with the virus of Colorado tick fever—one reacted with a typical attack, the other was found to be immune as the result of an experimental attack which occurred five months previously. Both of these persons 27 days after the defervescence of the one who was attacked and a normal volunteer were inoculated intradermally with serum from a dengue patient. All three responded with clinically typical dengue.

Two other volunteers were inoculated with dengue serum, and six days later had attacks of dengue-like fever lasting six days. Twenty-seven days after defervescence these persons and a normal volunteer were inoculated with the virus of Colorado tick fever. All three reacted with typical attacks of the disease.

The clinical features of the experimental attacks of the two diseases were remarkably similar except that no rash occurred in any of the cases of Colorado tick fever. The authors point out that different strains of the same disease agent may vary to some extent in their immunological properties so that if other strains had been used the results might not have been the same.

In spite of the obvious clinical relationship between the two diseases it would hardly be expected that they should be immunologically identical, in view of their being transmitted by different vectors—one case from man to man and in the other presumably from a lower animal to man.]

The authors refer to Bullis fever which like Colorado tick fever is associated with tick bite—they state that its aetiology appears to be different and that a further paper on the subject is in the press—they also promise a paper on the absence of immunological relationship between Bullis fever and dengue.

John W. D. Morgan

## PLAGUE.

MAGROT E & BRISON J. A propos d'une épidémie de peste dans un élevage de cobayes. [Plague Epizootic among Breeding and Experimental Guinea-pigs.] *Bull. Soc. Path. Exot.* 1946 v 39 Nos. 3-4 119-21.

An account is given of an epizootic of plague among laboratory guinea-pigs in the course of an epidemic of plague in which rats were the source of the infection. There were peculiarities in the epizootic which seem to have some significance. At first it was not recognized to be plague. On autopsy the guinea-pigs presented no characteristic lesions of organs, cultures were negative and microscopic examination of spleen smears showed only small round corpuscles some of which stained solid and some were vacuolated. These rounded bodies were Gram-negative and it was not until the epizootic became more fatal that typical bacillary forms of *P. pestis* appeared and cultures became positive. The authors put out the suggestion that these rounded bodies may be the only forms of *P. pestis* present in diagnostic smears of lymph nodes in the benign forms of plague and at the end of an epidemic. Cultures of the corpuscular forms when obtained, took some 6 to 8 days to appear at room temperature.

W. F. Harvey

MAGROT E. Le traitement de la peste bubonique par les sulfamides (sulfadiazine) [Treatment of Plague by Sulphadiazine.] *Bull. Soc. Path. Exot.* 1946 v 39 Nos. 3-4 113-19.

That the epidemic was due to a virulent strain is apparent from the facts that all untreated non-vaccinated persons died, and that inoculated guinea-pigs

died in 30 hours. Treatment apart from adjuvant and symptomatic therapy consisted of antiplague serum or sulphadiazine. Penicillin had proved useless experimentally in guineapigs and was therefore not tried. The sulphadiazine was given orally every four hours day and night in a large volume of liquid, with at least 20 gm. sodium bicarbonate daily to keep the urine alkaline. Originally the dose of sulphadiazine was 24 or even 30 gm. on the first day and this was gradually diminished during 10 to 15 days. The first dose was subsequently reduced to 24 or 21 gm. Treatment with serum alone appeared unavailing and there seemed to be little distinct advantage in combining serum with the sulphadiazine. Of the 28 persons treated with sulphadiazine two died a case mortality rate of only 7.14 per cent.

H. F. HARRY

## CHOLERA

GREIG E. D. W. The Treatment of Cholera by Intravenous Saline Injections with particular reference to the Contributions of Dr Thomas Aitchison Latta of Leith (1832) *Edinburgh Med J* 1946 May v. 53 No. 5 236-63. [18 refs.]

There are many reminders in this article of how our standard therapy has been built up or originated. Transfusion of saline solution in cholera was introduced to the profession by Doctor Latta of Leith when cholera reached Edinburgh from Newcastle early in 1832. The pandemic had started in Bengal in 1817 and for the first time reached Europe. It is sometimes difficult to follow the reasoning for old-time methods of treatment and this is illustrated here by reference to such therapy for cholera as actual cautery, bastinadoing the feet, suffocating under a feather bed. The treatment introduced by Dr Latta against considerable opposition however was based on scientific argument. He had read a report by O'Shaughnessy in the *Lancet* of the analysis of blood in cholera patients showing the great loss of water and of its neutral saline ingredients. After several trials he decided to supply the deficiency direct into the circulation and he described his solution as artificial serum. It was prepared by saturating water with protoxide of nitrogen holding in solution half a drachm of muriate and eight grams of subcarbonate of soda to the pound (pint) of water. Other details were included in the treatment which we have learnt to know as important. He used vapour baths to maintain the body temperature and recommended that the injection fluid should have a temperature of 112°F because 100°F is too low. The effects on the patient were dramatically favourable—on the pulse, the cramps, the temperature, the respiration, the countenance, the anxiety, the thirst and the secretion of urine. In all 156 cases of cholera were treated and 25 recovered. None would it is considered have recovered otherwise. There is much else of historical interest in this article and honour is also done to the collaborators of Dr Latta, to whom it is fitting that we should pay tribute for the wisdom that they taught us. [This paper is also a pleasing contribution to medical literature and throws an interesting sidelight on some aspects of the medical background of the early nineteenth century.]

H. F. HARRY

seasonal swing and the organism can persist on the surface only during the rainy season. In drier climates treponemata appear more abundantly in the axilla popliteal space perineum and external genitalia. Lesions of the mucous membranes which were rare as long as the skin lesions were florid become more numerous in these conditions appearing as mucous patches snail tracks or kidney-shaped ulcers on the fauces palate or pharyngeal wall. Such is the treponematoses of Arabia and mountain areas today whilst Ramsay in Assam observed 20 years ago that heat and moisture appeared to be the main factors in producing the characteristic lesions of treponematoses in that area.

Treponematoses did not remain confined to torrid zones. During its migration north its character altered by changing its pattern from a juvenile non-venereal disease to one of adult venereal infection. The forces of environment made it difficult for the parasite to remain confined to the skin, and drove the eruption towards the mucosa of the mouth and vagina. In this manner sexual intercourse afforded the common channel of infection.

In a specially important section labelled *Christopher Columbus* the author pours scorn on the familiar recapitulated tale of the introduction of syphilis from the New World. It is argued that the evidence in support of this story is very weak and that it is absurd to suppose that by action of the comparatively small number of suspects involved, the seeds of an epidemic of syphilis of such magnitude or of such virulence could have been sown. Arguing from analogy is at best a risky procedure but the author is not deterred by this, and refers to the accepted views on the genealogy of the horse from *Eohippus* on which the evolutionary development of the modern animal is generally based. In much the same way all the intervening and transitional steps between yaws and pueras can be demonstrated in European history within the compass of a few centuries.

The remainder of this exhaustive paper is replete with the oft-quoted distinctions between yaws and syphilis the trend of which is to back up Jonathan Hutchinson's dictum whenever an Englishman contracts yaws abroad he comes home with syphilis.

A similar attitude is adopted in the consideration of pinta which is regarded as the depigmentation commonly associated with syphilis and yaws. The parasite *T. carateum* is indistinguishable either from *T. pallidum* or *T. pertenue*. Pinta starts out exactly as many other cases of juvenile treponematoses. It is not true to state that it is confined to Central and South America as it would seem that this depigmentation is prevalent in the whole American hemisphere. Lieberthal has found three cases in Chicago and it is reported from the Argentine. American observers in Guam are finding it there now. Therefore pinta may occur anywhere where there is treponematoses especially of the juvenile and untreated type. That aortitis adenopathy juxta-articular nodules and other late signs of spirochaetosis are found in association with pinta is considered sufficient to clinch the argument.

Finally there are four considerations which recommend the author's views of acceptance of treponematoses as a world-wide disease. The first is a classification of nomenclature by resolving several diseases into one. This is a usual procedure as exemplified in other diseases such as tuberculosis in its various manifestations plague (sylvatic and human) borreliosis (tick and louse-borne) and yellow fever (jungle and urban African and American). Such classification has resulted in a better understanding of these diseases.

Secondly the comprehensiveness of treponematoses tends to produce a new and less provincial attitude.

Thirdly research in treponematoses is now handicapped by compartmental thinking and the assumption that yaws and syphilis are different diseases is a

barrier to any comprehensive programme. Yaws has much to offer as a field for study of the ecology and biology of the treponema.

Lastly if treponematoses is a disease of all mankind it should be recognized as such by epidemiologists, health officers, social hygienists and civil governments and such questions as sanitation, social habits, economics and laws are involved. Different educational procedures should be integrated. It is an illusion to hope for a syphilis-free civilization while yaws remains rampant in wide areas of the world.

[We have presented the author's views in an unbiased manner. He acknowledges himself quite patently as a disciple of that staunch unitarian, the late Admiral Charles S. BUTLER whose *Syphilis Sive Morbus Humanus* (1941) is so well known. No doubt equally cogent arguments can be advanced against this view. But that the present affords a good occasion to review the subject as a whole which has been so thoroughly and eloquently done in this treatise there can be little doubt.]

Philip Manson-Bahr

FLOCH H. & DE LAJUDIE P. Traitement pratique du pian par la pénicilline en suspension dans l'huile d'olive. [Treatment of Yaws by Penicillin suspended in Olive Oil.] *Institut Pasteur de la Guyane et du Territoire de l'Inini*. Publication No 115. 1945 Oct. 8 pp.

Solutions of sodium penicillin in distilled water, in saline or in 5 per cent glucose lose their activity within 48 hours even when kept in the cold; moreover when administered they are rapidly excreted. The authors found that in olive oil the drug could be kept for 10 days in a refrigerator and still be active and also that by being suspended in oil it remained longer in the body.

In practice 100 000 Oxford units are shaken for 10-15 minutes in 10 cc. of the oil previously sterilized in an autoclave. Four cases of yaws are recorded in which about 15 000 units were injected intramuscularly each day for 7 days, a total of a little over 100 000 units. By the third day the lesions had cleared or were fast disappearing and by the end of a week clinical cure was complete but serologically the Meinicke and Vernes reactions remained unchanged or were slightly reduced and continued so during subsequent periods of observation [but these were short: two months in two patients and only one month in the other two].

H. Harold Scott

## LEPROSY

IBARRA PÉREZ R. & GONZÁLEZ PRENDES M. A. Incidencia de la lepra en Cuba según la raza. [Racial Incidence of Leprosy in Cuba.] *Rev. Sifilografía, Leprología y Dermatología*. Marianao, Cuba, 1946 v 3 No 1 19-24 [11 refs.]

[It is difficult to reconcile the statements in the letterpress of this article with the figures presented in their support.] The authors claim at the outset that Cuba differs from other Latin American countries in that there is no half-caste population from crossing of the Spanish blood with that of the original indigenous inhabitants because the latter were exterminated in the 16th century. Nevertheless the percentage of half-castes from admixture of white and negro bloods is high. Whites number 3 553,312 (74.4 per cent. of the whole), negroes 463 226 (9.7), half-castes 743 115 (15.5) and Chinese 18,929 (0.4 per cent.). The lepers among these number respectively whites 1 649 [4.6 per 10 000], negroes 340 [7.3], half-castes 408 [5.4] and Chinese 30 [15]. In the face of

these figures [the totals only are given not the incidence by population] the authors claim that "race is not a predisposing factor because the incidence is the same among the different races composing the population." The slight increase among the black and yellow races is due, they say to economic and hygienic conditions—the people living in poor ill-fitted dwellings devoid of sanitation and overcrowded they are badly fed and predisposed to disease by the presence of malaria syphilis tuberculosis and parasitic infection. The authors next proceed to estimate the incidence exclusive of Oriente Province in which the population is given as 1,362,489 and they show that among the whites there are 1,313 cases [4.8 per 10 000] among the negroes 181 [8.0] among half-castes 236 [6.1] and among Chinese 28 [17.4]. They conclude from this that "the slight increase in the non-white races is due to the causes mentioned above." Lastly they give analogous statements on Oriente itself 337 lepers among 835,360 whites [4.0 per 10 000] 159 among 161 712 negroes [9.8] 172 among 356 532 half-castes [4.8] and 2 among 2,885 Chinese [6.9].

Commenting on these figures the authors state "The increased percentage of negro lepers occurs exclusively at the cost of the diminution in the white population. The half-castes and the Chinese retain the same percentage incidence." [It will be seen that the figures do not bear this out. In the Tables given the totals and the percentages of the whole are stated, not the morbidity by race. The figures given (by the abstractor) in square brackets have been calculated on the total figures in the text.]

H. Harold Scott.

TRESPALACIOS F. & GONZÁLEZ PREYDES M. A. Primeros síntomas y edad probable de contagio en lepra. Estudio de 315 casos aislados en el Hospital San Lázaro de la Habana. [Earliest Symptoms and Probable Age of Infection in Leprosy. *Rev. Sifilografía, Leprología y Dermatología* Marianao Cuba 1946 Jan. v 3 No 1 38-48.]

This record is based on a study of 315 patients in the San Lázaro Hospital, Havana. 233 were males 82 were females. 200 were whites 46 were negroes 50 were half-castes and 19 were Chinese. 262 were Cuban born 53 were from abroad.

Sometimes the first symptoms appeared suddenly (after months or even years of incubation) as for example a rhinitis with epistaxis at other times and more commonly insidiously with maculae or some cutaneous manifestation—erythema pigmentation or an achromic patch. In a Table giving the first symptoms it will be seen that 60 started with erythematous maculae, 25 with infiltration of the ears, 23 with patches of anaesthesia 17 with pigmented maculae the same number with systemic symptoms such as headache fever lassitude etc. ROGERS and MITCHELL, in an analysis of 252 cases found achromic maculae and anaesthetic patches as the first symptom in 188 or 74.7 per cent. In 206 patients (63 per cent) the symptoms appeared first before the age of 25 years 37 within the first 10 years of life the largest number in any single year was 28 in the 20th. The probable age when infection was contracted is also given in quinquennials the figures up to age 50 years being 3 31 60 68 45 30 20 20 9 and 13. [In another table six are said to have contracted the disease "soon after birth, in the first year of life."] The average age of contagion worked out at 18 years and the appearance of symptoms at 23 years. Of the total, 253 (80.3 per cent) suffered from the lepromatous form 49 (15.5 per cent) from a "non-characteristic or non-specific type" and 9 from the tuberculoid type [these total 311 not 315. During 1945 there were 31 deaths at the hospital 15 patients escaped, four were released on parole and there were 16 re-admissions.]

H. Harold Scott

JAGUETI DEL POZO G. La ginecomastia en la lepra. [Gynaecomastia in Leprosy] *Revista "Fontilles"* Valencia. 1946 Jan. No 4 283-95 4 figs. on 1 pl. [29 refs.]

RODRIGUEZ PASCUAL, C. Alteraciones nasales en la lepra. [Nasal Changes in Leprosy] *Revista Fontilles* Valencia. 1946 Jan. No 4 297-303 8 figs on 2 pls. [19 refs.]

DUEÑAS C & ABAD R. Serología de la lepra. [Serum Reactions in Leprosy] *Revista Fontilles* Valencia. 1946 Jan No 4 307-18 1 fig [28 refs.]

Three tests carried out with the serum of lepers are recorded. Either's complement fixation, Rubino's test with sheep's cells and Muchow and Levy's flocculation with leproma extract.

Sera from 249 patients with various types of leprosy were tested and the results are summarized thus —

International Classification	Number of Patients	Reac- Eitner — Posi- tives	Per- cent.	R. Rubino — Posi- tives	Per- cent	R. Muchow — Posi- tives	Per- cent
L1	2	—	—	1	50	2	100
L2	43	13	30.2	28	65.1	35	81.3
L3	61	19	31.1	42	68.8	51	83.6
N1	6	—	—	1	16.6	1	16.6
N2	16	5	27.7	13	72.2	13	72.2
N3	52	10	19.2	39	75	38	73
L2 N2	20	10	50	15	75	19	95
L2 N3	15	7	46.6	8	53.3	13	86.6
L3 N2	6	3	50	6	100	6	100
L3 N3	28	14	53.8	22	84.6	24	92.3
Total	249	61	32.5	175	70.2	202	81.1

With the Muchow and Levy test 81.1 per cent of the specimens were positive in some degree. The percentage distribution of positive results according to intensity of reaction is shown in the following table —

	+	++	+++	++++
L1	—	100	—	—
L2	16.2	32.2	23.2	11.6
L3	16.3	32.7	24.5	9.8
N1	16.6	—	—	—
N2	16.6	22.2	27.7	5.5
N3	5.7	25.0	30.7	11.5
L2 N2	10.0	50.0	45.0	10.0
L2 N3	—	20.0	47.3	20.0
L3 N2	—	—	33.3	66.6
L3 N3	—	7.6	45.3	38.4
Total per cent	10.4	25.3	30.5	14.8

These same sera were tested also for syphilitic and tuberculous reactions. For the former the Wassermann, Hecht, M.R.R., II, Kahn, Leinoff and Hinton (1933).



for the latter the Bestredka Daranyi and the Matefi. The authors conclude that among those of the same clinical type of leprosy the number and intensity of the reactions depend on the length and severity of the disease and that when the results of the leper sera coincide with those of the syphilitic tests both being positive there is probably a dual infection of leprosy and syphilis.

H. Harold Scott.

GUILLEN PRATS J & GOMEZ LUCAS R. Penicilina y lepra. [Penicillin in Leprosy. *Revista Fontilles* Valencia. 1946 Jan. No. 4 305-6.

The sodium salt of penicillin has been tried in a severe case of leprosy  $L_2$  with, so far good effect. The patient was a man of 43 years who had suffered from the disease for 16 years. His nose and ears were much enlarged by numerous lepromata, eyebrows gone, interstitial keratitis in both eyes especially the left, lepromata of shoulders, thighs and hands many confluent, oedema and infiltration of legs and feet. Bacilli were present in the nasal mucus and in the skin lesions. Red cell sedimentation 65 mm in one hour 110 in two hours. The penicillin was injected intramuscularly 10 000 Oxford units every three hours. Early injections caused febrile reactions disappearing in 24 hours, there was much local pain. By the third day the patient stated that he felt better and the vascularization of the conjunctiva and cornea was less. After 300 000 units the oedema of the feet and legs was reduced, the lepromata of the shoulders were smaller, he was much more cheerful and no longer suffered from insomnia. For 12 days the drug could not be obtained and the treatment had to be suspended. It was then resumed till he had had two million units. With this new series the early injections caused even greater febrile reaction than had the first but this reaction ceased in 36 hours and was never serious enough to call for suspension of the treatment. By this time the lepromata were reduced, oedema of the feet and legs was no longer observed, eye lesions were less marked and the euphoria continued as the patient was convinced of the improvement. The blood sedimentation rate was now 42 and 81 in one and two hours respectively. The amelioration had continued for 1½ months at the time of report. The authors acknowledge that this interval is short and think that higher doses should be given before the final assessment of the value of penicillin is made but so far they are favourably impressed by its action in leprosy.

H. Harold Scott

DE WILDEMAN E. A propos de médicaments antimépreux d'origine végétale. IV. Des *Strophanthus* et de leur utilisation en médecine.

This book is reviewed on p. 874

### HELMINTHIASIS.

GAMA, C. & DE SA, J. M. Esquistosomose medular (Granulomas produzidos por ovos de esquistosoma *Mansoni* (*Schistosoma Mansoni*) comprimindo a medula epicono cone e cauda equina—Paraplegia flácida) [Schistosomiasis of the Spinal Cord. Granuloma due to Ova of *Schistosoma mansoni* pressing on the Lower Spinal Cord.] in *Facul de Med. Bahia* 1944-45 v. 4 187-231 6 figs. [234 refs.]

Spinal symptoms have been recorded more than once in patients infested with *Schistosoma* but rarely has the cause been proved to be the helminth or its ova. DAY and KENAWY recorded a case in 1896 [see this *Bulletin* 1896

v 33 951] in which *S. haematobium* was the agent and there is another by HOFF and SHABY in 1939 [this *Bulletin* 1940 v 37 147] in which intestinal lesions were present and ova of *S. haematobium* found in the urine. In the latter case ova were not found in the spinal cord and all that can be said is that 'myelitis with mental disturbance occurred in a patient infested with *S. haematobium*'.

*S. japonicum* ova have also been found in the human brain [noted in BUIKE and FORSTER's *Handbuch der Neurologie*].

The case here recorded is that of a man aged 42 years with signs of flaccid paraplegia. His father had died of tuberculosis and several relations had had cancer. The paraplegia came on when he was in good general health and comparatively rapidly with pain in the loins and legs, formation retention of urine and faeces and loss of patellar abdominal cremasteric and plantar reflexes. The blood showed an eosinophilia of 16.3 per cent. [no details as regards totals of leucocytes are given and the percentage as stated adds up to 119.4]. Radiological examination after injection of lipiodol indicated obstruction beginning at the 6th dorsal vertebra and extending to the 12th where it became complete. A little later complete blockage of the spinal canal was found to be at the level of the 2nd lumbar vertebra.

Operation was decided upon and a swelling was found at this level. It was thought at first to be cystic but puncture did not draw off any fluid. A portion was taken for section and the tumour removed. It was found to consist of five small nodules in the centre of each of which was a foreign body which proved to be an ovum of *S. mansoni*. The patient was treated with founadin stibosan stibemyl anthiomaline and when these could not be obtained, with tartar emetic in 1 per cent solution and deep radiotherapy. There was good improvement within three weeks voluntary movements were returning in the toes and leg muscles and even before this he was regaining control of the bladder.

The actual source of infestation was not determined with certainty. The patient had bathed in waters in which the intermediate host *Australorbis glabratus* or *Planorbis olivaceus* was known to be present in 1926 and in 1941 1943 and 1944 and after the first at all events he had suffered from severe intestinal disturbance and frequent attacks of diarrhoea.

H. Harold Scott

GONZALEZ RINCONES P. *Stibioterapia per os* [Antimonial Medication by Mouth.] *Gac Med de Caracas* 1945 Sept. 15 v 53 No 17 127-41 11 figs. & 2 charts.

There are obstacles to administering tartar emetic by mouth because the gastric juice breaks it down since the HCl is stronger than the tartaric acid of the antimony potassium tartrate and more toxic compounds are formed. On the other hand there are drawbacks to intravenous administration. The salts are changed by heat and are difficult to sterilize in children and in some women the vein is not always easy to find, the patient has to attend at the doctor's surgery and this he often fails to do regularly.

The author has therefore aimed at finding some way of administering the drug by mouth without causing intolerance or signs of antimony poisoning. He has had pastilles made combining the drug with atropine 1/20 mgm. to every cgm. of the tartar emetic to counteract its stimulant effect on the vagus and adding a small proportion of vitamin B<sub>1</sub> (thiamin) and coating the whole with keratin to allow it to pass undecomposed into the intestine. He has used these for treatment of infestations by *Schistosoma mansoni* observing by X-ray the passage of the pastilles until they are dissolved and absorbed in the large intestine. Two cases are quoted and X-ray photographs are reproduced showing the progress of the pastilles. He gave four tablets (or pastilles)

the first day two doses of two each 8 on the second, 8 on the third 10 on the fourth (all colic and tenesmus had disappeared by this time) 12 on the fifth, and so on. By the 10th day 120 pastilles had been taken and, in all, 1.2 gm. of the drug. All clinical signs had cleared. Slight gingivitis with salorrhoea and a metallic taste indicated that the drug had been absorbed. The maximum dose in a day should be 2 ggm. per 10 kilos given in two or three doses in the 24 hours  
*H Harold Scott*

JANSEN G. Experiências sobre a profilaxia da esquistosomose mansoni no estado de Pernambuco. [Nota prévia. Prophylaxis of *Schistosoma mansoni* Infection in the State of Pernambuco. Preliminary Note.] *Brasil Medico* 1946 Mar 18 & 25 v 60 Nos. 20-21 177-8 3 figs.

This account deals with the Catende Municipality where was installed the first centre for combating schistosomiasis in Brazil.

Preliminary examination of the faeces of 6,539 persons showed that 3,482 (52 per cent) were positive. For initial experiment 50 patients were subjected to tibia intramuscularly and a like number to each of antimonyl, stibetine and 1 per cent. tartar emetic all administered intravenously. The numbers cured were respectively 11 23 37 and 49 cure implying three consecutively negative examinations.

Treatment was now started in earnest and up to December 1945 [the date of beginning the work is nowhere stated] of 1,348 receiving tartar emetic 1,159 (86 per cent) were cured of 292 receiving stibetine intramuscularly 42 (14.3) of 169 receiving it intravenously 97 (56.8) of 12 receiving antimonyl intramuscularly 5 were cured of 117 intravenously 39 (33.3) of 50 receiving stibien intramuscularly 11 (22 per cent.) Altogether of 1,868 patients treated 1,353 (68 per cent) were cured. No details of the composition of these drugs are given.

Tanks for washing clothes and public baths were installed and also house latrines for of 1,252 registered houses 424 had no sanitary installations of any kind.

Examination of the vector *Australorbis centranutalis* in various waters was carried out in July 1943 and again in December 1945. In 1943 of 732 from the Rio Piranga 10 were positive of 607 from the Rio Panelas 16 (or 1.32 and 2.63 per cent. respectively) in 1945 the numbers examined were 64 and 90 and the numbers positive 0 and 2 respectively lime having been applied in the interval.  
*H Harold Scott.*

LOBO R. A profilaxia da esquistosomose na Bahia. [Prophylaxis of *Schistosomiasis* in Bahia. *Brasil-Médico* 1946 Jan. 5 & 12, v 60 Nos. 1/2, 8-14.

Schistosomiasis mansoni constitutes in parts of Brazil, a scourge as serious as malaria nevertheless the Health Authorities "do not or pretend they do not see how serious the question is." In the past six years 1940-45 the local Laboratory returns of examinations for ova have been 26.6 40.0 32.5 32.3 24.0 and 43.7 per cent. positive. The author adds "Of a total of 661 examinations made 83 were positive—32 per cent." [If these last figures are correct, and they refer to 12 consecutive years the total is very small and the percentage is not 32 but 12.5.] Another table shows 2,223 examinations with 372 positive (16.7 per cent.) of which 1,594 were from males with 237 (18 per cent.) positive and 629 from females 85 (13.5 per cent.) positive.

Preventive measures suggested are along the usual lines. Establishment of Sanitary Posts for free treatment of patients installation of privies at all

schools propaganda by handbills lectures cinema films elimination of *Planorbis* from the waterways and relief of poverty malnutrition and over crowding  
H Harold Scott

LIGER & SCHEIDYER, R. Kystes hydatiques chez les indigènes Nord-Africains. [Hydatid Disease in North Africans.] *Semaine des Hôpitaux de Paris* 1946 July 21 & 22, No 27 1280-84 8 figs

DAVIES J A. Echinocecal Cyst arising from the Prostate *Canadian Med Ass J* 1946 Mar & 54 No. 3 268-71 1 fig

POST-GRADUATE MED J 1946 July & 22, No 249 203-4 Casoni Test. A Review

BERBERIAN D A. Treatment of *Hymenolepis nana* Infection with "Acranil." *Amer J Trop Med* 1946 May & 26 No. 3 339-43 [15 refs]

25 cases of *Hymenolepis nana* infection in children were treated by a synthetic acridine derivative Acranil. The night before the administration of Acranil the children were each given 0.1-0.2 gm. Calomel as aperient. The following morning Acranil was given on an empty stomach in 0.1-0.5 gram doses according to age. Three hours later a saline purge was administered. Treatment with Acranil was continued in smaller doses for three more days without any further purgation. 23 out of 25 children treated by this method remained free of worms for 14 days

BROWN H. W. The Use of Gentian Violet in Children infected with *Ascaris lumbricoides*. Reprinted from *J Pediatrics* 1946 Feb & 28 No 2 160-64 [14 refs.]

"1 Gentian violet therapy for ten consecutive days did not produce findings suggestive of migration of 4 *lumbricoides* or of intestinal or pharyngeal obstruction in twenty treated children. It appears therefore that gentian violet is not a specific irritant to *Ascaris*

2. A 37 per cent. reduction in the *Ascaris* egg count following gentian violet therapy suggests that this substance is slightly effective against *Ascaris*

BROWN T McP STIFLER, W C. Jr & BETHEA, W R. Jr Early Filariasis. *Bull. Johns Hopkins Hosp* 1946 Mar & 78 No 3 126-54 9 charts. [31 refs.]

This paper deals with the early clinical manifestations of filariasis as determined by the study of three groups of American servicemen—two of these groups served in the South Pacific islands (Tonga tabu and Woodlark) and the third, a control group had served in New Guinea, where manifestations of filariasis in American troops have been slight or had had no tropical service. These same cases have already been the subject of extensive reports by HODGE, DENHOFF and VANDER VEER [this *Bulletin* 1945 & 42 1020] and by BEHN and HAYMAN [this *Bulletin* 1946 & 43 762]. The present account does not materially add to the information already published and should be consulted in the original in conjunction with the other papers by those interested.

A R. D Adams

OLIVEIRA E. de S. Elefantase e estados elefantinos. (Notas de Cirurgia—Bahia, 1941) [Elephantiasis and Elephantoid Conditions.] *An Facul de Med Bahia* 1944-45 v 4 111-31 45 figs. [17 refs.]

The author gives details of the history and of the general clinical state and the local conditions of 9 cases of elephantiasis three each of the foot and leg the scrotum and the vulva. This is followed by a brief consideration of other growths with which elephantiasis might be confused for example hypertrophy of the breast molluscum tumours of the testicle large hernias even rhinophyma. Finally line drawings show the steps of operative treatment. The paper is almost entirely a surgical one. The illustrations are clear.

H Harold Scott

HAWKING F & BURROUGHS, Ann M. Transmission of *Leishmaniasis carinii* to Mice and Hamsters. [Correspondence.] *Nature* 1946 July 20 98.

KUITUMEN EKBAUM E. Phenothiazine in the Treatment of Enterobiasis (II) *Canadian J Pub Health* 1946 Mar v 37 No 3 103-13. [22 refs.]

Phenothiazine was given to 1,275 subjects (900 children and 375 adults) infested with *Enterobius vermicularis* and the results of this treatment were estimated by means of the N.I.H. swab. Before and after the treatment the blood haemoglobin of 25 children and 9 adults was estimated.

The ages of the subjects who came from all social levels ranged from three months to 78 years. Eleven children were less than 1 year old and 8 adults were 60 years old or older. Those under 15 years old are called children those over 15 years are called adults. Before treatment NIH swabs were taken on five consecutive mornings if eggs of *E. vermicularis* were found, treatment was given. During the second week after the end of treatment, 7 NIH swabs were taken on five consecutive mornings. When the first course of treatment was not effective treatment was repeated four weeks later. Diagnostic swabs were taken from 2,505 subjects (1,350 children and 1,125 adults) and phenothiazine was given to 1,275 (900 children and 375 adults). Post treatment swabs were taken from 790 (534 children and 206 adults) and the results given are based on these.

The phenothiazine used was supplied by the Connaught Laboratories and was refined and made into 0.5 gm tablets by SIEBENMANN [see SCHMITZER, SIEBENMANN and BETT this *Bulletin* 1942 v 39 882]. The author emphasizes the necessity of using highly purified phenothiazine.

Two dosage scales were tried. Scale A was 2.5 to 9 gm. for children in proportion to their age and 9 gm for adults given over four to six days. This scale caused toxic reactions especially in small children and it was abandoned. Scale B was therefore used, and was given over a period of 4 days. This scale was as follows—

Under 2 years	0.25 gm. per day total 1 gm.
2 to 3 years	0.5 gm. 2 gm.
4 to 5 years	0.75 gm. 3 gm.
6 to 7 years	1.0 gm. 4 gm.
8 to 9 years	1.25 gm. 5 gm.
10 to 11 years	1.5 gm. 6 gm.
12 to adult or over 15 years	1.75 gm. 7 gm.

For small children the tablets were crushed and mixed with food or orange juice. Other subjects were advised to chew and swallow the tablets. Extra fluid and avoidance of constipation were advised during treatment. Tables show the results of treatment.

Dosage scale B was given to 584 persons (408 children aged 7 months to 15 years and 176 adults over 15 years). The swabs of 327 (80.2 per cent.) of the 408 children were negative after the first course of treatment; those of 76 children (18.6 per cent.) after the second course and 5 (1.2 per cent.) children needed a third course. Of the 176 adults 150 (85.2 per cent.) gave negative swabs after the first course, 20 (11.4 per cent.) gave them after a second course and 6 (3.4 per cent.) needed a third course.

The toxic reactions are discussed in detail under the following headings —

**Anaemia** — Reduction of the haemoglobin level was the commonest evidence of this and was sometimes so severe that emergency treatment was required. The case histories of three girls aged 16 months, 8 years and 2 years respectively are given to illustrate this form of toxic reaction. Blood transfusions were given successfully to all three. The haemoglobin values of 25 children and 9 adults were estimated; all were given the dosage scale B, the first estimation being done before the first dose and the second on the fifth day after the last dose. The results showed that two children had a decrease of 3 gm. per 100 cc. of blood, four a decrease of less than 2 gm., 13 a decrease of less than 1 gm., while two showed no change and two showed slight increase. Of the nine adults tested, two showed a decrease of more than 2 gm., one a decrease of 1 to 2 gm., four a decrease of less than 1 gm., and two showed no change. The author refers to the work of MILLER and ALLEN [this *Bulletin* 1942 v 39 781] and of BERCOVITZ *et al* [this *Bulletin* 1943 v 40 929] who also found anaemia after administration of phenothiazine.

**Skin Reactions** — These were neither serious nor common. They included skin rashes, pruritus and oedema.

**Fever** — Other authors have reported a rise of temperature during treatment with phenothiazine. The present author reports a temperature of 100°F in a girl aged 6 years after one dose of phenothiazine and a temperature of 102°F in an adult female after one dose of 1.75 gm. Treatment of both these subjects was discontinued.

**Miscellaneous reactions** were slight pain in the abdomen in two children; several mothers reported pallor and decline of appetite during treatment of children. The author points out that various workers have used very variable doses of phenothiazine and he claims that all the serious toxic reactions reported in the literature have occurred after doses above his dosage scale B, although sometimes large doses have had no ill effect. Thus MANSON BARR [this *Bulletin* 1941 v 38 516] gave 7 to 40 gm. and ELLIOTT [this *Bulletin* 1943 v 40 702] gave 24 gm. Both these authors however gave a laxative with the phenothiazine and may thus have avoided toxic reactions. Some of the toxic reactions experienced by the present author were, he thinks, related to previous ill health and it would have been wiser to have reduced the dose and to have repeated it if necessary or to have waited until the health improved. [It would appear wise to raise the haemoglobin level especially before phenothiazine is given.]

Discussing precautions that should be taken, the author says that phenothiazine is more toxic than gentian violet but is more effective and is apparently tolerated by a larger number of individuals than gentian violet. It also requires a shorter period of treatment and is easily given to small children who cannot swallow gentian violet tablets. The phenothiazine must be highly purified; the patient should be in fair general health; constipation during treatment should be avoided; the drug should be discontinued at once if toxic reactions appear and it should not be repeated before 3 to 4 weeks after the first course. Pregnancy and lactation seem to be no bar to its use, but supervision of such patients is necessary. Discussing the treatment of families with phenothiazine

It is possible that thiamin lack is the one aetiological factor which accounts for both these diseases. At first it seemed a typical outbreak of beriberi, although the explosive character suggested that it might be epidemic dropsy.

*Philip Manson-Bahr*

PROC. ROY. SOC. MED. 1946 May v 39 No 7 357-60 (Sect. of Med. 9-12)  
 Discussion Nutritional Neuropathy in Repatriated Prisoners of War from the Far East. CLARKE C. A. & SNEDDON I. B. COLLIMAN E. R. SPILLANE J. D. KIRMAN B. D].

Drs Clarke and Sneddon reported some of the neurological signs found in men who had been released from Hong Kong (see *Bulletin of Hygiene* 1946 v 21 527). Some patients developed fresh neurological signs in hospital while eating a full diet supplemented by adequate amounts of thiamin parenterally. This fact was part of the evidence put forward by them in support of the theory that the neuropathy was not caused by simple lack of the vitamin B complex. In their opinion the syndrome was due to an anti vitamin or toxic factor present in the rice that inactivated what little thiamin was present in the diet. The thiamin deficiency was rendered more severe by the low protein intake that prevented adequate synthesis by bacteria in the gut. Changes in the nervous system appeared to be irreversible.

Dr Colliman described an outbreak of beriberi amongst East African troops whose diet consisted largely of lightly milled rice which in its uncooked state contained theoretically adequate amounts of thiamin. It was found that the rice which was old and showed surface contamination with a variety of moulds lost over 70 per cent of its thiamin during cooking whereas similar freshly milled rice lost only 30 per cent. [See also COLLIMAN *et al.* above.]

Dr Spillane summarized the clinical features of the nutritional neuropathic syndromes he had observed in prisoners of war during the past few years.

Dr Kirman reported that there was no increase in the incidence of psychosis amongst released prisoners who passed through India and none of the few psychotics seen showed signs of pellagra.

*H. E. Harding*

SIMPSON J. "Burning Feet" in British Prisoners-of War in the Far East. *Lancet* 1946 June 29 950-61.

Large bodies of Allied troops in Java capitulated to the Japanese in March 1942. Signs of deficiency disease which soon affected half of the prisoners developed after four months showing first as lesions of the mouth and scrotum. Shortly after these signs of pellagra and aridobla inosis had become manifest on a large scale a few men began to report sick with "burning feet" and during the following 3 months 10-12 per cent. of the prisoners had this complaint.

Most of the sufferers showed exaggerated knee and ankle jerks but no ankle clonus nor extensor plantar response and no spasticity. Early hyperaesthesia in the feet and lower legs was usually replaced by hyposaesthesia both sensory alterations showed a patchy distribution. No ataxia incoordination or loss of joint sense was demonstrated. The condition commonly became so severe as to dominate the life of the sufferers. Treatment with vitamin A ( $\frac{1}{4}$  oz red palm oil daily for 4-6 weeks) produced no improvement. 10 patients given 10 mgm. thiamin daily for a month showed no benefit. Giving the kacang hijau bean (*Phaseolus radiata*) in doses of 150 gm. daily cured the syndrome in 4-6 weeks. This bean is reported to be a rich source of vitamins B<sub>1</sub> and B<sub>2</sub>. In other camps the syndrome was cured by yeast or marmite.

Associated with burning feet but appearing a little later local eye irritation developed, followed closely by blurring of the vision and loss of visual acuity. After a rapid onset the visual upset usually remained stationary or tended to

improve very slowly About 10 per cent of those with burning feet developed retrobulbar neuritis visual defects occasionally developed without the peripheral pains but the two conditions were usually associated. Cure of the burning feet syndrome did not affect the visual condition

*H E Harding*

**HARRISON G F** Nutritional Deficiency, Painful Feet, High Blood-Pressure in Hong-Kong *Lancet* 1946 June 29 961-4 1 fig

Although many other conditions were met with in prisoners-of-war in Hong Kong the outstanding symptom almost throughout the Japanese occupation was painful feet In the early days the pain was so severe that the only drug that gave relief was morphine in  $\frac{1}{2}$  grain doses by mouth. Later the intensity of the pain diminished and less potent drugs were effective The pains were accompanied by lost or diminished sensitivity to touch pin prick heat and cold and often by loss of joint sense and sense of position in the toes.

Eleven patients were given 10 ml. of 10 per cent calcium gluconate intravenously on several occasions. They appreciated a flush spreading down the body and if this sense of warmth reached the feet the pain was sometimes relieved for a time Some of the patients who were given 20 mgm. nicotinic acid subcutaneously or 100 mgm. by mouth obtained relief from pain and one patient experienced almost immediate complete relief for about 5 minutes after inhaling the contents of one ampoule of amyl nitrite Exercise had a beneficial effect on the pain and those who conscientiously walked as much as possible each day made a speedier recovery than those who could not or would not make the effort Recovery took years rather than months despite daily doses of 20 mgm. nicotinic acid subcutaneously 3-5 mgm. thiamin chloride by mouth, yeast drinks and other foods containing vitamin B complex [Much of this is contrary to the findings of Simpson—see above.]

At least 19 per cent. of the 400 patients suffering from malnutrition had at some time—usually at an early stage—a high diastolic blood pressure. In many of these the systolic pressure was also raised. In a few patients simultaneous records were made each week of the blood pressure in arm and leg Almost always the systolic pressure was higher in the leg than in the arm and in one instance was 50 mm. Hg higher Not all patients with a raised blood pressure had pain.

The author suggests that the cause of the pain and of the high diastolic pressure was spasm of the blood vessels in the legs.

*H E Harding*

**BLANKENHORN M A, VILTER, C. F, SCHEINKER I M & AUSTIN R. S** Occidental Beriberi Heart Disease *J Amer Med Ass* 1946 June 29 v 131 No 9 717-26 1 fig [Refs in footnotes.]

Heart disease as a manifestation of beriberi was recognized in 12 patients admitted to the Cincinnati General Hospital from 1940 to 1945 All the patients were chronic addicts to alcohol but this substance is not considered to be a direct cause of the condition. The ages of the patients ranged from 33 to 67 years and only one was a woman. Five patients died in hospital and one died 3 months after being discharged. Two patients recovered with rest in bed, a full diet and digitalis one of these died 3 months later The response to large doses of thiamin was rapid in only one patient the others recovered slowly

The authors think that the criteria for diagnosis of the condition have been set too high, and propose the following as aids to its recognition (1) insufficient evidence of other aetiology (2) a diet deficient in thiamin for at least three months (3) signs of neuritis or of pellagra (4) enlargement of the heart with sinus rhythm (5) dependent oedema (6) a raised venous blood pressure



Percentage absorption figures were calculated directly from the difference between the amount of fat ingested and that found in the faeces over the comparable period. When the percentage absorption is calculated in this manner it was found to be 95 or over in the controls. In practice it was found that cases with percentage absorption of less than 85 invariably showed associated signs and symptoms confirming a fat-absorption defect.

Seventy to eighty per cent. of faecal fat is normally present as fatty acid or soap. The degree of splitting of neutral fat is interpreted as an index of pancreatic function but this is not invariably so because even after complete pancreatectomy in man lipolysis still occurs for lipase exists in the gastric and intestinal juices. The percentage hydrolysis of fat in the faeces cannot therefore be regarded as a reliable index of normal pancreatic function.

The interpretation of changes in the chemical characteristics of faecal fat is at present unsatisfactory. The authors were unable to demonstrate any constant features in the faecal fat in their series. Usually about half the split fat is present as soap although considerable variations are found in case to case.

It has been suggested that the rapid rate of passage of intestinal contents through the alimentary tract might constitute an important factor in the production of a fault in fat absorption. In those cases of diarrhoea in which charcoal passed through the alimentary tract within seven hours of ingestion, fat absorption was normal. It is therefore concluded that when intestinal hurry can be demonstrated in these cases the colon is primarily involved and consequently defective absorption of fat cannot be attributed to lack of time.

In addition to the investigation of the amount of fat in the faeces the absorption of fat may also be investigated by examination of the blood during the post absorption period either by chemical analysis or by chylomicrograph. In the normal subject a characteristic lipaemia can be demonstrated in the systemic blood during four hours after ingestion of fat and it was a striking feature of many of the cases of defective fat absorption that whilst fat balance tests indicated that 70-80 per cent. absorption had occurred, there was little or no change in the blood-fat.

The constantly flat chylomicrograph curve and correspondingly low value for blood fat obtained in chemical analysis are difficult to explain, unless it is assumed that the fat is leaving the intestine by some pathway other than the thoracic duct and systemic blood.

P. Manson-Bahr

KARAMCHANDANI P. V. & HYDER G. Analysis of 342 Cases of Sprue in Indian Troops. *Indian Med Gaz.* 1946 Jan. v 81 No. 1 11-13

"Para sprue" corresponds to what has so far been known as "incomplete sprue" "chronic jejuno-ileal insufficiency" or a vitamin B deficiency syndrome allied to sprue.

The authors view of the pathological process is as follows.—With faulty intake and faulty absorption the stress initially falls on the delicate columnar intestinal epithelium and the symptoms evoked depend upon the site and extent of the damage. When the duodeno-jejunal region is attacked, there may be deficiency of bile flow, failure of emulsification, and increase of split fat in the stools because it cannot be absorbed, or there may be deficiency of pancreatic secretion resulting in high total fat content in the stools. When the ileum is affected, the fat content in the stools is normal, and the diarrhoea is of the irritative type (enteritis) but when the colon is involved blood and mucus may appear in the evacuations.

The post-mortem appearances in two typical cases are recorded. The small intestine is described as wasted, with destruction of villi and desquamation of the epithelium.

A series of 242 cases of the sprue syndrome was observed during a period of 2½ years. These were grouped as follows—dyspepsia and diarrhoea 88 dyspepsia diarrhoea and glossitis 96 the same signs with addition of anaemia 54 the same with excessive split fat in the stools 4

The majority of cases fell within the age-group 20-25 the duration of the disease bore no relation to its severity. Thirty-one cases had associated amoebic infection but six only had blood and mucus in the stools

Treatment at first consisted of 8 oz. of milk given every 2 hours from 6 a.m. to 10 p.m. This was increased to 10 oz. during the next 4 days. This diet provided a Calorie value of 1 625 with 82 gm. protein 90 gm. fat and 120 gm. carbohydrate. During the second and third weeks additions were made to the diet which was increased to 2 560 Calories with 97.70 and 458 gm. of protein fat and carbohydrate respectively. During the next three weeks it was augmented to 3,200 Calories with 154.114 and 596 gm. protein fat and carbohydrate respectively. Vitamin-containing foods fruit juices and liver preparation were given

Those with concomitant amoebic infection were given routine treatment by emetine Yatren emetine bismuth iodide and Amoebiarson

Of the 242 cases 129 were cured and discharged to duty 22 were improved and placed permanently in category C 67 were improved placed in category C but relapsed 22 were not improved and were invalided out of the service. Two patients died.

P Manson Bahr

SPIES T D FROMMEYER W B GARCIA LOPEZ G LOPEZ TOGA R. & GWINNER, Georgia. Haemopoietic Action of 5-Methyl Uracil (Thymine) in Tropical Sprue. *Lancet*. 1946 June 15 833-5 2 figs.

Since synthetic 5-methyl uracil (thymine) produces a striking haematological response in Addisonian pernicious anaemia in relapse and as the bone marrow of this condition is indistinguishable from that associated with the macrocytic anaemia of tropical sprue four patients suffering from relapse of the latter disease were given 7.5 gm. of the drug twice daily by mouth for 9 to 16 days. In each case there was a definite haematological response parallel to although less dramatic than that which follows the administration of synthetic folic acid. Reticulocytosis began on the fourth or fifth day reaching a peak on the eighth or ninth day of treatment and was followed by an increase in the erythrocytes and haemoglobin. On the day after the peak reticulocytosis the bone marrow consisted largely of normoblasts with almost complete obliteration of the megaloblastic arrest found before treatment. Clinical improvement was manifested by an increase in appetite and strength resolution of the glossitis and disappearance of the burning and soreness of the tongue and mouth. Although the stools did not become fully formed, they showed as early as the fourth day of treatment in one case a return towards normal. X-ray examination of the gastro-intestinal tract showed a substantial decrease in intestinal motility in spasm and dilatation and in the amount of puddling of barium after administration of the drug. Glucose tolerance tests indicated that intestinal absorption improved after therapy.

F Murgatroyd

DARBY W J & JONES E. Treatment of Sprue with Synthetic L casei Factor (Folic Acid, Vitamin M). *Proc Soc Exper Biol & Med* 1945 Nov v 60 No 2, 259-60

This is a report of the first two of the three cases of sprue treated with synthetic L casei factor which were recorded by DARBY JONES and JOHNSON (cont)

[the *Bulletin* 1946 v 43 667 the authors state that "there appears to have been published no previous experiences with this factor in the treatment of sprue"  
J F Corson.

CARRUTHERS L B Chronic Diarrhoea treated with Folic Acid. *Lancet* 1946 June 8 849-50

Four severe cases of hypochromic anaemia were treated with 40 to 60 mgm. folic acid daily for five to seven days without any noteworthy improvement in the anaemia but in two of the patients who had chronic diarrhoea an immediate and definite improvement in the stools occurred. This led the author to try the effect of folic acid on six other cases of chronic diarrhoea of vaguely determined aetiology. In these cases the stools became normal, or approximately so within two to five days of starting the treatment. He therefore suggests that in any long standing diarrhoea a nutritional factor prolongs the production of abnormal stools and that folic acid appears to correct this defect.

F Margatroyd.

JENSEN H Results of Experimental Resections of the Small Intestine on Dogs. (Experimental Enteroprival Sprue.)

This book is reviewed on p. 971

## HAEMATOLOGY

ZUELLER W W & OGDEN Faith V Megaloblastic Anaemia in Infancy A Common Syndrome responding specifically to Folic Acid Therapy. *Amer J Dis. Children* 1946 Mar v 71 No 3 211-43 7 figs. (1 coloured on 1 pl.) [Refs. in footnotes.

Macrocytic anaemia commonly occurs in infancy as a result of a specific dysplasia and dysfunction of the bone marrow developing in the absence of an essential haematopoietic principle. Clinically the outstanding feature is extreme pallor with weakness loss of appetite and irritability fever vomiting and diarrhoea are common complaints. In the series of the 25 patients studied, many of the infants had cough, convuls or both for several weeks before admission to hospital and the beginning of the illness was usually referred to the onset of these symptoms. In several cases petechiae had been noted by the parents. On examination, a soft systolic murmur could often be heard over the praecordium, and slight cardiac enlargement was evident. The liver was invariably increased in size but the spleen was palpable in only 10 of the patient. In no case was there any appreciable lymphadenopathy. Half the patient were underweight six had clinical signs of scurvy and 19 had fever of variable degree.

The disturbance in erythropoiesis was shown in the bone marrow by the prevalence of young basophilic and polychromatic cells limitation of mitotic activity abnormal karyokinesis an abnormal nuclear structure lobulation and distortion of the shape of the nuclei an increased tendency to demargination, and an increase in the size of the cells and in the relative amount of cytoplasm at all levels of maturation. The pattern corresponded basically to that seen in pernicious anaemia in relapse and was typical of alterations produced by lack of a so-called maturation factor resulting in multiplication of cells confined mainly to primitive levels. Similarly leucopoiesis showed constant qualitative changes leading to a relative decrease in the number of mature cells.

The peripheral blood showed always a severe anaemia with haemoglobin levels near 5 gm. per 100 cc. and often below 3 gm. Reduction of the red blood cells was often even more pronounced, and the colour index was usually but not invariably well above unity. The mature erythrocytes appeared well filled with haemoglobin and this was borne out by the mean corpuscular haemoglobin concentration. Polychromasia and punctate basophilia were invariably present to a slight degree and Howell Jolly bodies and Cabot rings were often seen. The percentage of reticulocytes was usually small and obviously did not account for the macrocytosis of the blood. Nucleated red cells were always found but sometimes only after prolonged search. The white cell count was below 10 000 per cmm in most cases despite the presence of fever or other signs pointing to infection and in some cases a frank leucopenia existed. Neutropenia was common being as a rule moderate but sometimes pronounced. The neutrophils were usually much larger than normal being of two basic types with transitions between the extremes. The first was characterized by excessively large nuclei of the metamyelocyte type often showing budding twisting and the beginning of segmentation while the granulation of the cytoplasm was uneven and suggested immaturity. The second type showed fully developed granulations of the cytoplasm and excessive segmentation of the nuclei with long tenuous filaments connecting the lobules. The platelets were reduced in number often markedly and the thrombocytopenia accounted for the prolonged bleeding time inadequate clot retraction and the haemorrhagic manifestations shown by several of the patients.

Infections and other complications were common and multiple transfusions were often necessary. These factors limited the number of cases suitable for the evaluation of specific therapy to 12. In these latter the effect of crude or purified liver extract given parenterally and that of folic acid, appeared to be identical whether the folic acid was given orally or parenterally in the form of concentrates or as synthetic material. A second reticulocyte response could not be produced by liver extract when folic acid had been given first and *vice versa*. Since liver contains folic acid the identity of the therapeutic effect raises the question whether for this form of anaemia liver extract owes its efficacy to its folic acid content. Between the third and fourth day after beginning treatment with folic acid in dosage of from 5 to 100 mgm. daily the reticulocytes in the blood began to rise and shortly afterwards the haemoglobin level and the red blood cell count began to improve. The reticulocytes usually reached a considerable peak in another three to four days and then decreased rapidly while the haemoglobin level and the red cell count continued to rise. The neutrophil leucocytes also increased and the hypersegmented forms gave way to normal cells within seven to sixteen days sometimes a slight eosinophilia appeared. The platelets also increased in number soon after therapy was started. The bone marrow underwent a striking transformation and assumed a normal pattern within a few days. Unless other illnesses interfered, the patient's appetite rapidly improved, the colour returned and the irritability disappeared. Splenomegaly and hepatomegaly although often persisting for some weeks after treatment eventually disappeared. In a follow-up period ranging from 3 to 20 months there were no recurrences of this type of anaemia in any of the patients who did not succumb to complications.

Inadequate diet and probably conditions interfering with proper absorption in the intestinal tract are possible factors producing the deficiency leading to this anaemia of infancy but it seems doubtful that these are the only factors concerned while the frequency of infections was striking. It is suggested that infections and nutritional deficiencies are aetiologically significant, while race age and possibly prematurity and maternal anaemia are predisposing factors.

F. Murgatroyd

ZUELLER, W. W. Folic Acid Therapy in the Anaemias of Infancy and Childhood. *J Amer Med Ass.* 1946 May 4 v 131 No 1 7-8 1 chart.

This paper is another report on the effect of folic acid on the anaemia with a megaloblastic type of blood formation in the bone marrow which is not uncommon in white infants under the age of 18 months. [See ZUELLER & OGDEN above.] The characters of this anaemia are as follows. There is a severe normochromic anaemia usually but not invariably with macrocytosis there is a tendency toward leucopenia and neutropenia with giant metamyelocytes macropolycytes and hypersegmented neutrophils in the peripheral blood the platelets are diminished, sometimes to a severe degree and there is an increased tendency to bleeding and the bone marrow is frankly megaloblastic, resembling that of pernicious anaemia in relapse. Splenomegaly is common, but not constant some infection is usually present the nutritional history is usually poor and histamine-fast achlorhydria is often present although it does not persist after the anaemia is cured.

Twelve patients suffering from such an anaemia were treated with folic acid in synthetic form or by oral administration of concentrates rich in *Lactobacillus casei* factor the dosage of folic acid varying from 5 to 20 mgm. daily and the period of treatment from eight days to three weeks.

Three patients died of severe infections before the effect of the folic acid could be evaluated. In the remaining nine an unequivocal response was obtained, characterized by a reticulocytosis within a few days of starting treatment, a rise in the red cell count and haemoglobin level and a return of the bone marrow picture to normal. No relapses were observed in a follow-up period of ten months.

Folic acid therapy gave completely negative results in 18 children with anaemia of prematurity five with hypochromic microcytic anaemia, one with Mediterranean anaemia, two with chronic hypoplastic anaemia one with subacute myelogenous leukaemia, one with acute lymphatic leukaemia and one with sickle cell anaemia. In none of these patients was a reticulocyte response obtained nor did improvement of the anaemia occur even when large doses of folic acid, up to 50 mgm. daily, were given parenterally. The prophylactic use of folic acid from birth onwards over a period of months in premature infants did not prevent the development of anaemia comparable to that observed in control patients. A combination of folic acid and iron therapy did not increase or accelerate the effect of the latter in cases in which iron was indicated.

F. Murgatroyd

WILSON H. E. SASLAW S. & DOAN C. A. The Effect of Folic Acid (*Lactobacillus casei* Factor) in Nutritional Hematopenia of Monkeys. *J Lab & Clin. Med.* 1946, June v 31 No 6 631-42, 5 figs. [23 refs.]

DAVIS J. E. On the Mechanism of Action of Folic Acid and Liver Extract in the Treatment of Anemia. [Correspondence] *Science* 1946 July 12, 37-8.

MERSKEY C. & BASARD E. Chronic Haemolytic Icterus resembling Acholuria Jaundice occurring in an African Native. *South African Med J* 1946 May 11 v 20 No 9 230-33.

An African native complaining of pains in both legs attributed to osteitis of the tibiae and with an enlarged spleen thought to be due to chronic malaria, was found on investigation to present features suggestive of acholuric jaundice. The erythrocyte fragility tested by saline solutions was increased, there was a slight reticulocytosis a positive indirect van den Bergh reaction, and increased urobilinuria without anaemia or evidence of haemolytic crisis. Owing to lack

of facilities it was not possible to measure the mean corpuscular diameter but in blood smears the cells appeared microcytic and dense which together with a mean corpuscular volume not far removed from normal was presumptive of spherocytosis. Some years previously the patient had had a severe illness lasting three months during which he had had many small haemorrhages from his nose and mouth and since that time he had had occasional febrile attacks. He had never noticed any jaundice and such of his family history as was available revealed nothing of significance. As he was free from symptoms he was discharged from hospital with a diagnosis of acholuric jaundice. He was subsequently twice admitted to hospital and the haematological findings again supported this diagnosis. The illness which brought him to hospital for the third time was a characteristic haemolytic crisis. For the first time he showed an appreciable anaemia and a well marked reticulocytosis. The bone marrow was typically erythroblastic and this reaction as well as a leucoblastic irritation could be detected in the peripheral blood films. During his crisis his red cell count dropped by nearly two million cells per cmm with only a slight increase in jaundice. There was a doubtful report of malarial parasites being present in his blood but this was not confirmed, no significant auto- or hetero-haemagglutinins or lysins could be demonstrated, and no lytic drugs had been given.

The question as to whether the disease represented a congenital or acquired type of acholuric jaundice is open to some doubt but the comparative mildness of the condition is suggestive of the former. Against this however must be weighed the fact that the patient had probably been subjected to prolonged malarial infection which might have lead to an acquired haemolytic anaemia. The authors believe this to be the first case of chronic haemolytic icterus to be reported in an African native.

F. MURGATROYD

SEN A. K. Argemone Oil. *Indian Med Gaz* 1946 Mar \ 81 No 3 126-8  
1 pl

*Argemone mexicana* is found practically everywhere in India since it will grow wild and in poor soil. The seeds being abundant and cheap they are used alone or with others as adulterants of mustard seed and argemone oil as an adulterant of mustard oil is known to be one perhaps the only cause of epidemic dropsy.

The author here describes three chemical tests for the oil as used at the Bengal Public Health laboratory Calcutta.

(1) The *Nitric Acid Test*—Pure nitric acid is thoroughly mixed by shaking with an equal quantity of the oil. On being set aside for the layers to separate the acid layer becomes red. When adulteration in small quantity up to 1 per cent. is present the colour is yellow and with increasing adulteration this deepens to orange and finally to red. Fallacies of this test are Sesame oil gives a yellow colour and artificial colouring matter may have been added. The test is therefore to be recognized only as a preliminary one.

(2) The *Cupric Acetate Test*—Five cc. of the suspected oil and 5 cc. of a known good oil are placed in two test tubes. 1 cc. of glacial acetic acid is added to each and the mixture is well shaken. Next 2 cc. of 3 per cent. cupric acetate in distilled water dissolved by heating in a water bath are added and the whole well shaken to mix and placed in a boiling water bath for 15 minutes with frequent shaking to prevent separation of layers. In the control tube the copper solution is sky blue. If argemone oil is present it is greenish with adulteration as high as 10 per cent. it is yellowish-green. This test is confirmatory of the nitric acid test and will detect adulteration of 0.5 per cent.

(3) The *Ferric Chloride Test*—This test as now used at the Bengal laboratory is a modification of that of S. N. SARKAR described in 1941 [see this *Bulletin*

ZUKER W W Folic Acid Therapy in the Anemias of Infancy and Childhood. *J Amer Med Ass* 1946 May 4 v 131 No 1 7-8 1 chart.

This paper is another report on the effect of folic acid on the anaemia with a megaloblastic type of blood formation in the bone marrow which is not uncommon in white infants under the age of 18 months. (See ZUKER & OGDEN above) The characters of this anaemia are as follows. There is a severe normochromic anaemia usually but not invariably with macrocytosis there is a tendency toward leucopenia and neutropenia with giant metamyelocytes, macropolyrhytes and hypersegmented neutrophils in the peripheral blood the platelets are diminished sometimes to a severe degree and there is an increased tendency to bleeding and the bone marrow is frankly megaloblastic, resembling that of pernicious anaemia in relapse. Splenomegaly is common but not constant some infection is usually present the nutritional history is usually poor and histamine-fast achlorhydria is often present although it does not persist after the anaemia is cured.

Twelve patients suffering from such an anaemia were treated with folic acid in synthetic form or by oral administration of concentrates rich in *Lactobacillus casei* factor the dosage of folic acid varying from 5 to 20 mgm. daily and the period of treatment from eight days to three weeks.

Three patients died of severe infections before the effect of the folic acid could be evaluated. In the remaining nine an unequivocal response was obtained, characterized by a reticulocytosis within a few days of starting treatment, a rise in the red cell count and haemoglobin level and a return of the bone marrow picture to normal. No relapses were observed in a follow-up period of ten months.

Folic acid therapy gave completely negative results in 18 children with anaemia of prematurity five with hypochromic microcytic anaemia, one with Mediterranean anaemia two with chronic hypoplastic anaemia one with subacute myelogenous leukaemia one with acute lymphatic leukaemia and one with sickle cell anaemia. In none of these patients was a reticulocyte response obtained, nor did improvement of the anaemia occur even when large doses of folic acid up to 50 mgm daily were given parenterally. The prophylactic use of folic acid from birth onwards over a period of months in premature infants did not prevent the development of anaemia comparable to that observed in control patients. A combination of folic acid and iron therapy did not increase or accelerate the effect of the latter in cases in which iron was indicated.

F Mergatroyd

WILSON H E SASLAW S & DOAN C A The Effect of Folic Acid (*Lactobacillus casei* Factor) in Nutritional Hematopenia of Monkeys. *J Lab & Clin Med* 1946, June v 31 No 6 631-42, 5 figs [23 refs]

DAVIS J E On the Mechanism of Action of Folic Acid and Liver Extract in the Treatment of Anemia. [Correspondence] *Science* 1946 July 12, 37-8

MERSKEY C & BASKIND E Chronic Haemolytic Icterus resembling Acholuric Jaundice occurring in an African Natives. *South African Med J* 1946 May 11 v 20 No 9 230-33.

An African native complaining of pains in both legs attributed to osteitis of the tibiae and with an enlarged spleen thought to be due to chronic malaria was found on investigation to present features suggestive of acholuric jaundice. The erythrocyte fragility tested by saline solutions was increased, there was a slight reticulocytosis, a positive indirect van den Bergh reaction, and increased urobilinuria, without anaemia or evidence of haemolytic crises. Owing to lack

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1942, v 39 711-1. The modifications and the reasons for them are considered in detail and those interested should consult the article—they are not very great. The author claims that the test in its modified form is simpler than the original, that the crystalline precipitate is obtained with so small an adulteration as 0.25 per cent., and that the acicular crystals are specific for argemone oil.

H. Harold Scott.

## VENOMS AND ANTIVENENES.

DUREX A. Les serpents venimeux du Congo Belge. 'Poisonous Snakes of the Belgian Congo. Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales. Mémoires. (Collection in-8°) 1946 v 13 No. 5 45 pp. 11 figs on 5 pls. [12 refs.]

In his introduction the author remarks that the poisonous animals of the Belgian Congo are not of much importance—that accidents due to them are few and hence—the problems to which they give rise are negligible in comparison with those arising from pathogenic organisms—worms and insects. To stimulate interest and research he has therefore produced this brochure—as the field for study is virgin soil waiting for discoveries to be made. The present work is introductory in nature. Snakes of the Belgian Congo belong to five families: Typhlopidae, Glauconidae, Boidae, Colubridae and Viperidae. Next he gives lists of Opisthophypha and Proterophypha Colubridae and Viperidae which are poisonous. Speaking generally about one third of the snakes in the Colony are dangerous—of 724 captured at Stanleyville 331 were *Boodon olivaceus*, 75 were *Chlorophis irregularis*, both aglyphous Colubridae, 220 *Couerus rhomboides* and 98 *Bilus nasicornis* Viperidae. Then follow some notes on 12 species—their size, habitats, feeding habits and, after general remarks on the poisons of Colubridae and Viperidae such as are found in all textbooks, he offers some observations on Congo species and the effects of their bites—both garnered from the reports of others. No original work is recorded.

This article would serve well as an introductory chapter to detailed investigation of the subject as stated in the title and in his conclusions the author asks for information on the following three points: (1) Return of cases of poisoning and abstract reports on the symptoms. (2) Geographical distribution of the poisonous snakes of the Belgian Congo. (3) Study of the venoms of those most common or most dangerous with a view to preparing antivenenes.

H. Harold Scott.

POLSON A. JOUBERT F. J. & HAIG D. A. An Electrophoretic Examination of Cobra Venoms. *Biochem J.* 1946 v 40 No. 2, 265-9. 8 figs.

SMITH H. M. Preliminary Notes and Speculations on the *Triseriatus* Group of Rattlesnakes in Mexico. *Univ Kansas Sci. Bull.* 1946 May 1 v 31 Pt. 1 No. 3 75-101. 23 figs. & 1 pl.

## DERMATOLOGY AND FUNGUS DISEASES.

HAILEY H. Treatment of Creeping Eruption (Larva Migrans). *Southern Med J.* 1946 May v 39 No. 5 371-2. 1 fig.

At a meeting of the Section on Dermatology and Syphilology, Southern Medical Association, Cincinnati, in November 1945 the author described four cases of creeping eruption treated by him with onion poultices.

The poultices were prepared by spreading white vaseline over a piece of gauze and adding finely grated onion in a thickness of about  $\frac{1}{4}$  to  $\frac{1}{2}$  of an inch the poultice being covered with waxed paper or some other impervious material. It was applied nightly for three to seven nights. In his limited number of patients the treatment proved as satisfactory as the use of ethyl chloride in similar patients.

The author claims that this treatment has the advantage of cheapness and freedom from pain as compared with ethyl chloride which had proved extremely painful.

In the discussion which followed, seven speakers quoted their experience in the treatment of larva migrans with such a variety of remedies as arsenicals, antimony compounds chrysarobin ethyl acetate ethyl chloride and carbon dioxide snow.

These opinions confirm the well known experience to which the author himself testifies that the large number of treatments for creeping eruption is good testimony to the fact that a better one is greatly to be desired. [Whether that desire has been satisfied by the treatment described would require considerably more evidence and the author's report has been made in the hope that other dermatologists will attempt to determine its true value. He has in any case added one more remedy to the already lengthy list of measures adopted against this distressing condition.]

H J O D Burks-Gaffney

NOVACOVICH G G Observations and Data on Prevention of Poison-Oak Dermatitis. *U.S. Nav Med Bull* 1946 June v 46 No 6 811-19 1 fig [15 refs.]

The so-called Poison-oak is a species of Poison Ivy *Toxicodendron diversiloba* though it has an oak like leaf it is not related to the oak in any way. It contains an allergenic oleoresin the same as that in poison sumac and Japanese lac trees. Injection of the antigen produces some degree of immunity but not great. Oral administration gives better results though the immunity is temporary it lasts for 5-6 months. It was found that about 2 cc. of the oil diluted and administered over a period of 8-9 months was sufficient. One method was to give as an initial dose 0.5 mgm. of ether-extracted residue and gradually to increase till at the end of 45 days the day's dose was 150 mgm.

Various antidotes and protectives were tried chlorinated lime antigas ointments perborate ointment among them. The best was found to be 10 per cent chlorinated lime in an ointment basis consisting of —

Cetyl alcohol	35.1
Stearyl alcohol	5.3
Cerestin	3.5
Castor oil	20.8
Mineral oil	21.9
DuPont WA pure	1.7
Sodium perborate	10.0
Boric acid	0.7

It inactivates (or destroys) the toxic principle and is also usable prophylactically.

H Harold Scott

WEIDMAN F D & GLASS F A. Dermatophytosis and other Forms of Intertriginous Dermatitis of the Feet. A Comparison of Therapeutic Methods. *Arch Dermat & Syph* 1946 Mar v 53 No 3 213-25 1 chart

There is acute need for a satisfactory means for keeping the feet of fighting men in good condition in which connection intertriginous dermatitis poses a large problem. As to specific curative agents dissatisfaction is general particularly

in respect to the recurrences that are so notorious. Thus far salicylic acid, iodine and chrysarobin are the anchors but the last two particularly chrysarobin are capable of producing a chemical dermatitis and hence should be employed only under expert medical supervision. In view of the urgent need of better chemotherapeutic measures against foot ringworm the authors undertook a carefully controlled experiment in treatment of intertriginous dermatitis on 117 life-sentence prisoners in a penitentiary. Six preparations were tested, as follows: (1) Cresatin Sulzberger (metacresylacetate) used at full strength. (2) boric acid foot powder (5 per cent. boric acid in talc). (3) ointment of benzoic and salicylic acids (3 per cent. salicylic and 12 per cent. benzoic acid in a petrolatum base). (4) "Iodolate" (iodocholeate) used as a 20 per cent. ointment as supplied by the maker. (5) Pomeio (potassium mercuric iodide in 1.2 per cent. aqueous solution). (6) Zephiran chloride (a mixture of alkyl dimethyl benzyl ammonium chlorides). All the medicaments were applied by the prisoners themselves according to mimeographed instructions and the results were classified as Cured "Nearly cured," "Improved."

Stationary and "Worse." Considering only the "cured" and "nearly cured" cases two preparations stood out apart from all the others in effective news: these were cresatin and the boric acid foot powder—the foot powder being nearly as effective as cresatin. When the improved results were added to the "cured" and "nearly cured," the salicylic-benzoic ointment entered the picture and all three preparations seemed to be about equally effective in causing improvement with satisfactory results in about three-quarters of the cases. This suggests that while the salicylic-benzoic ointment is as effective as the other two preparations in bringing about clinical improvement its action seems to stop short of cure: this tends to bear out the view sometimes expressed, that the effect of salicylic acid ointments is merely to remove the superficial epidermal scales. The results from preparations 4, 5 and 6 were frankly disappointing: in fact 28.5 per cent. of the patients treated with iodolate were rendered "worse" and in some of the cases severe reactions even amounting to suppurative or chemical dermatitis occurred.

The authors were not able to confirm the views of Lewis that *Trichophyton interdigitale* and *T. purpurum* cause distinctive lesions and that lesions caused by *T. purpurum* are specially resistant to treatment. On the contrary they obtained cures in 50 per cent. of the *T. purpurum* infections and in only 32.4 per cent. of the *T. interdigitale* infections. The *T. purpurum* infections were almost confined to men below middle age.

J. T. Duncan

GOMEZ, J. E. Tokelan in Guatemala. *Arch. Dermat. & Syph.* 1948 Mar., v. 53 No. 3: 243-8. 3 figs.

This paper gives a good account of the history and nomenclature of Tokelan disease (tinea imbricata) first described by William Dampier in the Philippines in 1688. In the South Seas the disease is associated with the warm and very humid climate of the coastal areas but in Guatemala it occurs most frequently at distances of 80 to 170 kilometres from the sea coast and at an altitude of 3 000 to 9 000 feet. Clinically and mycologically the Guatemalan disease is similar to that of the South Seas—it is commoner in women than in men and the predisposing factors seem to be malnutrition and neglect of personal hygiene. Treatment on the whole gave only disappointing results except in the case of sodium lodoxymolnulsulphonate which showed considerable promise and merits further trial.

To obtain clear photographs of the lesions the skin was rubbed with a compress saturated with 10 per cent. gentian violet, and the following day after careful washing only the diseased scales were found to retain the dye.

J. T. Duncan

MOORE M & ACKERMAN L V Sporotrichosis with Radiate Formation in Tissue. Report of a Case *Arch Dermat & Syph* 1946 Mar v 53 No 3 253-64 3 figs. [Refs in footnotes]

In the lesions of sporotrichosis *Sporotrichum schencki* is sometimes seen as a yeast like cell or a small collection of cells surrounded by eosinophil club-shaped bodies similar to those seen in actinomycosis and some other fungus diseases. The appearance in sporotrichosis is sufficiently rare to warrant publication of the case SPLENDORE who was the first to describe the appearance (in 1908) named the fungus *Sporotrichum asteroides* believing it to be a new species but the organism when studied in saprophytic life was found to be the typical *Sporotrichum schencki*. The club-bodies are probably formed by the host tissues although the species or the peculiar strain of the fungus parasite may be a determining factor in their formation. J T Duncan

WILLETT F M & WEISS A Coccidioidomycosis in Southern California Report of a New Endemic Area with a Review of 100 Cases. *Ann Intern Med* 1945 Sept v 23 No 3 349-75 8 figs [33 refs.]

Unsuspected exposure to infection by *Coccidioides immitis* during military training of United States troops in desert areas of California Texas Arizona and New Mexico has revealed hitherto unknown endemic areas of coccidioidomycosis. The diagnosis of infection rests chiefly on a routine use of the coccidioidin skin test a positive reaction occurring in a man on whom a previous test had given a negative result being accepted as satisfactory evidence of recent infection. Although a majority of the positive reactors are symptomless the authors were able to analyse the symptomatology of 100 cases of primary coccidioidomycosis in four of which (all negroes) the disease progressed to the grave disseminated form. Fever of some degree was present in 80 per cent of the cases and it lasted on the average less than a week. Chest pain usually aggravated by deep breathing or coughing in 73 per cent. cough in 64 per cent. was almost invariably non productive but the transient appearance of blood streaked sputum was noticed in 3 per cent. joint manifestations chiefly arthritis in 8 per cent. erythema nodosum in 4.4 per cent. and erythema multiforme in 2 per cent. (of 135 patients) malaise a vague symptom, in 43 per cent. anorexia was definite in 30 per cent. headache in 27 per cent. was of a generalized type, and was so severe, in some cases as to justify spinal puncture. chills occurred in only 12 per cent.

The X ray picture of the chest usually showed some degree of parenchymal infiltration ranging from a minimal lesion to consolidation often associated with hilar adenopathy and thickening and sometimes a pleural exudate. Pulmonary cavitation was detected in 6 per cent. of the cases and was always a late complication of the acute stage its typical thin walled character becoming apparent only after resolution of the surrounding consolidation. The lesions of bone were well-circumscribed areas of destruction with some tendency to bone proliferation and elevation of the periosteum.

Dermal sensitivity to coccidioidin is evidence of present or past infection. It is usually demonstrable in two to four weeks from the time of infection and it persists for an indefinite time. The reaction is apparently specific but it is absent in the earliest stages of the disease (two to four weeks) and in the state of allergy associated with severe disseminated disease. Eosinophilia is present in some degree ranging from 5 to 18 per cent. in most cases during the initial few weeks of the disease. Serum tests are of particular value both in diagnosis and prognosis a declining antibody titre being an indication of progressive recovery while a persistently high titre for complement fixation

suggests an unfavourable issue. As primary coccidioidomycosis is essentially a pulmonary infection the examination of the sputum (when obtainable) offers a means of diagnosis. However the spherules of *C. immitis* are difficult to detect even in specimens of sputum cleared by caustic potash solution and although the fungus was cultivated from the sputum of 61 per cent. of the present series of cases it was found by microscopy in only 28 per cent.

For a more detailed analysis this important paper should be consulted in the original.

J T Duncan.

## TROPICAL ULCER.

WEBB J G Tropical Ulcers and Penicillin. *Brit Med J* 1946 July 13 40-50.

It was to be expected that as penicillin became more widely available it would soon be added to the already imposing list of remedies which have been given a trial in the treatment of tropical ulcers.

In this paper the author describing the results of seven years' study of tropical ulcers in South China claims a remarkable response on their part to treatment with penicillin. The claim is however based upon 10 cases only.

The aetiology of tropical ulcer is discussed, and the clinical stages are described. The author accepts the specificity of *B. fusiformis* [*Fusiformis fusiformis*] as a causative organism and its disappearance as a criterion of cure. Six of the ten cases also showed the presence of mixed cocci. The age of the ulcers before treatment varied from 3 days to 6 months (in two cases the ulcers had relapsed after primary occurrences of five months and three years respectively).

Penicillin was given locally a solution of 500 units per ml being applied on gauze twice daily and by intramuscular injection of 15 000 units three-hourly up to a maximum of 90 000 units (except in mild cases).

Results were very good, the fever and inflammation subsiding in one to three days when the ulcer presented a smooth granulating surface. Further treatment was similar to that of varicose ulcers. The time of final healing is not recorded. The author enters a plea for the widespread use of penicillin as it becomes available.

[HAMM and QUARY (this Bulletin 1945 v 42 495) and MOREAU and QUARY (*ibid* 1946 v 43 378) described 18 and 19 cases respectively of tropical ulcer treated with penicillin with apparently very good results. It is a matter of some doubt whether the beneficial effects in all of these cases were due to elimination of the *F. fusiformis* or as appears to be more likely the destruction of the mixed cocci. The treatment merits wide trial, which will no doubt be forthcoming as supplies of penicillin become available.]

H J O D Burke-Gaffney

## MISCELLANEOUS DISEASES

MIRICK G S, ZIMMERMAN H M, MAYER G D & HUMPHREY A A.  
Melioidosis on Guam. *J Amer Med Ass.* 1946 Apr 20 v 130 No 16  
1063-7 8 figs.

This paper describes two cases of melioidosis in American service men, developing after some six months on Guam. Both cases ran an acute course terminating fatally after five and seven days respectively. At autopsy military

abscesses were present in the lungs liver spleen and kidneys. *Pf. whitmorei* was isolated from the blood stream on the 5th day of disease in the second case and from the visceral lesions in both cases *post mortem*. These strains grew readily on the usual media including Koser's citrate medium under aerobic conditions and produced acid but no gas from glucose and galactose in two days lactose mannitol, xylose maltose sorbitol and adonitol in six days and sucrose in nine days rhamnose dulcitol and trehalose were not fermented. Ammonia was produced from peptone nitrates were reduced to nitrites methylene blue was reduced and catalase reaction on inoculation into male guinea pigs produced a typical Strains reaction on inoculation into male guinea pigs. Systemic penicillin (a total of 200 000 units in the first case the amount in the second being unspecified) was without effect and laboratory tests showed that these strains of *Pf. whitmorei* were insensitive to as much as 35 units of penicillin per ml. Growth of an inoculum of about 1 000 bacteria in tryptose phosphate broth was however completely inhibited by sulphadiazine in a concentration of 15 micrograms per ml in 18 hours at 37 C.

S P Badson

HERBUT P A & KINSEY F R. Transitory Pulmonary Infiltrations (Loeffler's Syndrome) in Rabbits. *Arch Pathology* 1946 May 1 41 No 5 489-502 3 figs. [Refs in footnotes.]

Löffler when first reporting cases of what has since come to be known as Löffler's syndrome—eosinophilia with transitory pulmonary infiltration—stated that recovery took place in all so that no examination of the pathological changes was possible but it was thought that the lesion was a specific tissue reaction probably produced by a variety of antigens and comparable to erythema nodosum [sic] of the skin.

The authors have carried out experimental work on rabbits sensitizing them to horse serum by repeated subcutaneous injections then exposing the trachea and instilling horse serum intratracheally a single dose of 5 cc in one group and 0.5 cc hourly for 5-12 doses in one or two days in a second group. Systemic disturbance was slight but by X-ray pulmonary infiltrations were seen which cleared in 1-2 weeks the tracheal secretions contained eosinophiles and the submucosa of the trachea and bronchi was congested and oedematous and showed infiltration with eosinophiles but there was no blood eosinophilia as in human cases of Löffler's syndrome and the lung infiltrations were more persistent. The authors conclude that Löffler's syndrome is an allergic inflammation of the lungs and that one route by which the allergen invades is that of inhalation. [In view of the absence of eosinophilia and the longer persistence of pulmonary signs the condition produced in these experimental rabbits differs from Löffler's syndrome in man and the conclusion is therefore hardly justified.]

H Harold Scott

DERVISON W & EVANS W. Report of a Case of Multiple Idiopathic Haemorrhagic Sarcoma occurring in a West African Native. *Trans Roy Soc Trop Med & Hyg* 1946 June 1 39 No 6 521-2 3 figs. on 1 pl.

ALLEN J M. Noma treated with Penicillin. [Memoranda.] *Brit Med J* 1946 July 6 14

A record of three cases in which penicillin was of great value.

VAN DER WALT S J & STEYN D G Recent Investigations into the Toxicity of Plants, etc., No. XV *Onderstepoort J Vet. Sci & Animal Industry* 1946 Mar v 21 No. 1 45-55 3 figs.

"Of the 16 plants investigated the following four plants were according to the literature available to the authors for the first time proved to be toxic *Tetragonia Schenkii* Schinz. *Encephalartos Lehmannii* (E. & L.) Lehm. *Moraea trita* var *foliata* N.E Br and *Schizocarphus nervosus* (Burch.) F v d.M.

The toxicity of the pupae of *Melasma circophora* Meyr was also investigated."

WAHL, P N Needle Biopsy of the Liver Technique and Diagnostic Application. *Indian Med Gaz* 1946 Mar v 81 No 3 130-34 7 figs. (6 on pl.)

A plea for the taking of small portions of liver tissue by means of the Vim-Silverman needle as an aid in the diagnosis of obscure liver conditions. The bleeding time clotting-time, prothrombin-time and prothrombin concentration are first determined as a routine, and any serious tendency to bleeding passive congestion of the liver suspected liver abscess or suppurative cholangitis are considered to be contra-indications for the operation. Vitamin K is injected intramuscularly if the prothrombin concentration is 50-70 per cent. if lower than that the operation should not be done. It is also given to all patients with jaundice. The track for subsequent insertion of the needle is anaesthetized and the needle then is passed half an inch into the liver substance the trocar having been withdrawn the inner split-needle is passed into the cannula then the outer needle is advanced over the split-needle, to compress the latter and secure the piece of tissue and rotated once to cut the base of the core. With enlarged and palpable livers entry is made below the rib margin in front otherwise at the 6th or 10th intercostal space in the mid or anterior-axillary line.

Six cases are mentioned in which this biopsy examination assisted or confirmed clinical diagnosis and others are referred to e.g. one of lardaceous disease in a tuberculous patient in whom the liver condition had been thought to be cirrhotic.

H Harold Scott

## GENERAL ENTOMOLOGY

FAUST E C Modern Methods for the Control of Arthropod-transmitted Diseases. *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Dec. v 6, No 4 205-12

DAVID W A L Factors influencing the Interaction of Insecticidal Mists and Flying Insects. Part II. The Production and Behaviour of Kerosene Base Insecticidal Spray Mists and their relation to Flying Insects. *Bull Entom Res* 1946 May v 37 Pt 1 1-28 1 fig [17 refs.]

The author uses the apparatus described in a previous paper [this *Bulletin* 1946 v 43 679] to investigate production and behaviour of insecticidal spray mists. The following factors are discussed —

(1) Those concerned with atomization of the spray — Design and dimensions of the atomizing nozzle spraying pressure and air/liquid volume ratio viscosity surface tension and the density of the spray liquid.

(2) Factors concerned with passage of spray droplets through the air — Composition of the droplets size of the droplets and the influence of evaporation rate of fall of the droplets

(3) Properties of the mist in relation to insects at rest or in flight — Composition of the mists and their changes with time contamination of motionless and flying insects transit volumes of the latter

In the experimental section mists of different composition were sampled at various times after evolution. A quantity of kerosene or other oil dyed with Sudan III was sprayed into the cabinet and samples were collected from the mist (i) by a sintered glass funnel from which the dyed oil was recovered and measured colorimetrically or (ii) by a sliding impactor or a cascade impactor. The design of the slide impactor is described. These two impactors give indications of the drop-size distribution for all drops except the very smallest. The quantity of spray which fell to the floor was estimated by a glass plate from which the oil was washed and estimated colorimetrically. The results showed that —

(1) Increase in air pressure (7.5 to 20 lb/sq in.) for atomization produces a mist with a larger proportion of small droplets so that a smaller amount falls to the base in a given time.

(2) Pre-spraying of the chamber at the rate of 180 cc./1 000 cu. ft. greatly reduced the evaporation of the droplets of kerosene subsequently sprayed at 12.8 cc./1 000 cu. ft. and much bigger drops resulted. The theoretical saturation concentration of refined kerosene in air at room temperature is about 1 700 cc./1 000 cu. ft. so that the vapour slows down evaporation of droplets at quite a low fraction of the saturation value. Pre-treatment of this type with the non-volatile white oil P31 had no effect on the drop size of the subsequent mist.

(3) The mists produced by kerosene were compared with mists of the very volatile petroleum ether and the non volatile oil P31. The first evaporates to a mist of extremely small particles and only 5 per cent. is deposited on the floor after ten minutes compared with 20 per cent. of kerosene and 70 per cent. of P31. The drops of the P31 are generally of larger range than those of kerosene. (All oils were sprayed at a spraying pressure of 12.5 lb/sq in. and at the rate of 12.8 cc./1 000 cu. ft.)

The very fine droplets are too small to impact but slip round the air-stream past a flying insect. Consequently the mists of very small drops of insecticide dissolved in petroleum ether are less effective than the same quantity applied in kerosene. This difference is greatest shortly after spraying before the kerosene droplets have evaporated to very small dimensions.

(4) The addition, to a kerosene spray of 5 per cent. non volatile oil does not greatly increase the amount falling to the base in ten minutes but it does produce a mist of rather larger droplets. Consequently it is more effective in killing flying insects (as shown by tests with *Aedes aegypti*) since they pick up a larger dose of insecticide.

(5) An increase in the quantity of liquid sprayed from the rate of 12.8 cc./1 000 cu. ft. to double or quadruple this amount reduces the speed of evaporation of droplets and increases the proportion which falls to the base.

(6) By means of the sliding impactor the drop size distribution of sprays can be measured. Half a minute after spraying kerosene the drops range from 3 to 20 microns in diameter but these have all evaporated to less than 5 microns in four minutes. If however 5 per cent. non volatile oil is added, any larger droplets (up to 13 microns) can be preserved up to four minutes.



McGOVERN E. R., FALES J. H. & GOODHUE, L. D. New Formulations of Aerosols dispersed by Liquefied Gases. *J. Econom. Entom.* 1946 Apr v 39 No 2, 216-19 1 fig.

Tests of various liquefied-gas aerosol preparations against houseflies and mosquitoes were made in a Peet-Grady chamber. Aerosol formulae showing great improvement in toxicity over the original formula have been developed by increasing the non-volatile content. The original contained 2-4 per cent. non volatile material this can be increased up to 15 or 20 per cent. with improving efficiency. Above 20 per cent. however the efficiency definitely declines. This is probably because aerosols with low non-volatile content evaporate to minute particles too small to impact on the insects. Increasing the non volatile content enlarges the final size of the droplets and improves chances of wetting the insects. Above a certain size however the drops fall rapidly to the floor. Improvements in formula can also be made by adding more sesame oil or other synergist or by adding DDT or benzene hexachloride. Details of several effective formulae are given. *J. R. Bursine.*

GOODHUE, L. D. & RILEY, R. L. Particle-Size Distribution in Liquefied-Gas Aerosols. *J. Econom. Entom.* 1946 Apr v 39 No. 2, 223-6 6 figs.

A method of determining the particle size of liquefied-gas aerosols is described. The aerosol is projected into a settling chamber from a hole in the middle of the base and allowed to settle for two hours on to slides coated with mannitan monolaurate which is oleophobic and retains the oil drops as lenses. By various measurements the volumes of drops which produce lenses of different sizes can be estimated, and the numbers of each size can be counted. Distribution curves of particle size are given for aerosols of different composition. The most effective concentration of non volatile material seems to be about 15 per cent. From insecticidal tests it appears that drops of insecticide 2 to 10 microns in radius are the most effective in killing free-flying insects. *J. R. Bursine.*

GLASGOW, R. D. & COLLINS, D. L. The Thermal Aerosol Fog Generator for Large Scale Application of DDT and other Insecticides. *J. Econom. Entom.* 1946 Apr v 39 No 2 227-35 24 figs. on 2 pls.

Ordinary insecticide atomizers produce droplets of the order of 50 to 150 microns in diameter. The smoke generators employed for military purposes (screening) evolve drops of oil 0.5 to 0.75 microns in diameter but by suitable modifications they can be made to produce larger drops. A suitable size for insecticidal use appears to be about 10 to 50 microns. The authors have made some trials of two types of thermal fog generator for control of insects. [Very few observations are given the tests are described as successful etc. or "dead insects swept up for a week afterwards."] The two generators used in the trials were —

(1) The HOCHBERG-LA MER type which evolves droplets by the use of superheated steam and

(2) The TODD Thermal Generator which employs a temperature-controlled blast of hot air to atomize the insecticide

Successful non-residual control of houseflies mosquitoes "punkies" (gnats) blackflies stable flies etc. was obtained by the use of an aerosol produced from 5 per cent. DDT in kerosene used at the rate of 0.2 lb. of DDT per acre. This

type of aerosol was also used in buildings for control of cockroaches and clothes-moth larvae but the results are not clearly stated. *J R Bursine*

SCHROEDER, H O & LINDQUIST A W. Sprayers—for dispensing Concentrated Insecticides. *Soap* New York 1948 June 1 22 No 6 149-51 & 173 3 figs.

Small compact sprayers from  $\frac{1}{2}$  to  $1\frac{1}{2}$  inches in diameter and  $4\frac{1}{2}$  to 14 inches in length have been made for atomizing concentrated insecticides in household use. The sprayer plan consists of a cylindrical liquid tank containing the insecticide carried in a compression cylinder which slides up and down over the liquid cylinder. At the base of the latter is a leather washer valve

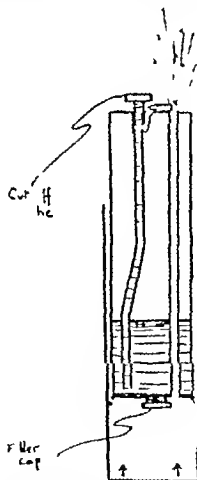


Diagram illustrating the essential details of the pocket size spray atomizer redrawn in simplified form from figure 1 in the original paper by Schroeder and Lindquist in *Soap*

in the centre of which is an oil resistant gasket for filling the liquid reservoir. The movement of the compression cylinder compresses air which is carried up through a tube going right through the liquid tank. The liquid insecticide is drawn up by suction from another tube which runs to the base of the liquid cylinder while the upper orifice is set at right angles to the air jet. The movement of the outer cylinder over the inner one thus generates the air to atomize the insecticide. When not in use a screw valve in the liquid tube is closed to prevent leakage whatever the position of the apparatus. *J R Bursine*

WIERSMANN R. & ZIMMERNAGEL R. Eine neue Methode zur Bekämpfung der Mückenbrut. [A New Method of controlling Mosquito Larvae.] *Gesundheit u. Wohlfahrt* 1946 June v 28 No 6 297-332, 6 figs. [28 refs.]

Methods of controlling mosquito larvae are briefly reviewed, and the qualities of an ideal insecticide for the purpose are enumerated. The main body of the paper deals with experiments with Gyron a powder preparation containing 5 per cent. DDT compounded for larvicidal use.

*Anopheles* larvae in water that has been dusted with Gyron become restless in five to ten minutes after fifteen to twenty minutes they frequently fall to the bottom and have difficulty in regaining the surface. Tremors begin and continue for a long time while the larvae finally are unable to leave the bottom. Similar signs of intoxication are shown by *Culex* larvae but less rapidly since owing to their position at the surface they are less readily contaminated by the powder.

Pupae of both types of mosquito are resistant to DDT applied in this way. This is because the insect in this stage is protected by the cast skin of the last larval stage in which it is lying. There is one part of the body in the abdominal region where the new cuticle is still in contact with the old one. This part is sensitive to DDT but normally is protected from the particles falling from the water surface because the abdomen is tucked under the body. If this position is disturbed, or if an emulsion of DDT is used, the pupae are killed.

From the outline area of the larva the amount of active ingredient which falls upon it can be calculated. Thus it can be estimated that with a dusting of Gyron at 2 gm. per sq. m. a larva receives only 0.001 mgm. of DDT. This dose is sufficient to incapacitate all *Anopheles* larvae in about two hours and all *Culex* larvae in four hours. The speed of action depends on the temperature. Experiments with *Anopheles* larvae showed that with a dusting of 3 gm. Gyron per sq. m. all larvae sank in two hours at 18-25°C. In three and a half hours at 16°C. in six hours at 13°C. and in ten to eleven hours at 6°C.

In nature it may happen that a pond dusted with Gyron will be cleared by the action of wind or rain after a certain period. Tests were therefore carried out to determine how long an exposure is necessary to result in the death of all larvae. Experiments were done at different temperatures using 3 gm. Gyron per sq. m. in all cases. After various times under the toxic dust, the larvae were removed in a pipette to clean tanks. It was found that *Anopheles* larvae were killed by the following exposures to Gyron films—20 minutes at 30°C. 25 minutes at 25°C. 35 minutes at 20°C. 55 minutes at 15°C. and 85 minutes at 10°C.

Experiments with various stages of larvae showed that the resistance increases with age from first stage to fully grown larvae. The latter were accordingly used in most of the experiments.

Tests were made with Gyron to determine its effects on aquatic organisms other than mosquitoes. A normal dusting was harmless to newts and water snakes and also to Crustacea such as *Gammarus*, *Cyclops* and *Daphnia*. Of the insects those forms which live on or visit the surface (water skaters, water beetles, etc.) were killed though, surprisingly enough, the bugs *Neops* and *Ranatra* were not affected when obviously contaminated.

Bottom-living forms were not harmed except in clean glass dishes, for they are normally protected by vegetation and detritus. Plants, coelenterates and protozoa were unaffected.

Comparative to atomic. It is done with various other mosquito larvicides to compare. Non-residual controls were used at concentrations of 5 per cent. and applicable flies etc. was 0 per sq. m. All were found to have some disadvantages. DDT in kerosene used was effective but is poisonous to mammals,

etc Phenothiazine (thiodiphenylamine) and hexachlorocyclohexane (crude Gammexane) are effective but soon lose their toxicity. Gesarol a horticultural preparation of DDT sinks too quickly to the bottom. None was as satisfactory as Gyron.

Several small practical trials on still lakes with Gyron are described in some detail. It is concluded that it should be applied at the rate of 3 gm. per sq. m. and this will prevent breeding of mosquito larvae for three to four weeks. Therefore two or three dustings should suffice to prevent breeding throughout the summer breeding season.

GOLDING F D A New Method of trapping Flies Bull Entom Res 1946  
May \ 37 Pt 1 143-54 2 figs J R Bursins

This new method consists of the use of Até adhesive the coagulated latex of the vine *Carpodinus hirsuta* found in Nigeria. This latex is mixed with some vegetable oil and produces the adhesive which is then applied to wire which are suspended in kitchens etc. The fresh substance appears to attract the flies after a week the viscosity decreases and many insects escape. [As a control measure this technique was of some value but with the use of residual DDT it is probably already obsolete.] It may be useful in making a survey of flies.]

Some interesting figures are given showing the flies captured at Ibadan. Houseflies mainly *Musca domestica* were trapped over two years in 17 kitchens. In all 272 498 flies were counted. The maximum catch occurred during the summer rains when the temperature was high and breeding accelerated and when desiccation was not a serious problem to the flies. Flies were captured throughout the day but in the greatest numbers at dusk. Flies were captured. Flies were also trapped in pig pens where *Stomoxys* made up about 27.5 per cent. of the total catch.

SMITH A. & GREAVES D P A Case of Myiasis due to Warble-Fly Larvae Brit Med J 1946 July 27 120-22, 3 figs [11 refs.] Kenneth Mellanby

A case due to *Hypoderma lineatum* contracted in England.

MICHENER, C D Observations on the Habits and Life History of a Chigger Mite *Eutrombicula batatas* (Acarina: Trombidinidae) Reprinted from Ann Entom Soc America 1948 Mar \ 39 No 1 101-18 34 figs on 5 pls. [12 refs.]

This mite is of interest mainly because of its relationship to the Trombiculids which transmit scrub typhus. This paper contains no new information of direct medical importance but various biological data are given which may assist those working on the disease-carrying mites. The life-history and its various stages are described in detail and the duration of these stages is also given. The eggs laid singly in damp soil develop in about four days but the larva remains another week in the shell. This is called the deutonymph. The active larva may take 14 days to find a host on which it remains from two to ten days. It is active for up to four days after feeding but then becomes quiescent as a protonymph. [This is often called the nymphophane by other authors.] This turns into the nymph whose active life is from 16 to 45 days. There is another week of inactivity as a preadult before the final moult. The adult lives up to 45 days. The food of the nymph and adult has not been determined but it is suggested that it may be fungal. The technique used is described. [For details see this Bulletin 1946 \ 43 797]

Kenneth Mellanby

JAYEWICKREME, S. H. A Note on the Breeding of Nymphs of the Trombiculinas (Acarina) Reprinted from *Ceylon J Sci. Section B Zoology* 1946 May 30 v 23 Pt. 2 85-8

Scrub typhus research has always been held up because of difficulties in the handling and breeding of the vectors in the laboratory. So far no really satisfactory technique of breeding the Trombiculid mites has been described, though several workers have suggested that they have discovered improved methods which, on further investigation, show little advance. The author of the present paper is less ambitious in his claims, and only sets out to show how to obtain the nymphal stage from the larva, a step which has often been accomplished before, but not with the same high percentage of success. Engorged larval mites were kept in glass cells on wet cellulose wadding. The larval skins could usually be correlated with the nymphs which emerged, an important step in obtaining a correct description of the various stages in the life-history.

Kenneth Mellanby

DE MEILLON B & DAVIS D H. S. *Pulex irritans* [Correspondence.] *Trans Roy Soc. Trop & Hyg* 1946 June, v 39 No. 6 544

In the flea survey of the Union of South Africa, *Pulex irritans* was found on rats and other rodents, dogs a pig and a calf.

EDNEY E. B. An Apparatus for handling Small Living Insects. *Bull Entom Res* 1946 May v 37 Pt. 1 83-7 3 figs.

This enables such insects as fleas to be sorted and examined, alive, under the microscope. With practice, an individual insect can be isolated ready to examine in 15 seconds. A suction pump glass and rubber tubing, wax and Canada balsam are all that is required. For details of the mechanism reference must be made to the original paper which cannot very well be summarized.

Kenneth Mellanby

SWARTS W B & WANAMAKER J F Skin Blisters caused by Venous Beetles. *J Amer Med Ass.* 1946 June 15 v 131 No. 7 594-5 4 figs.

The author states that more than 200 species of blister beetles have been found in the United States. The species depicted in this paper *Epicauta cincta* is about 1.5 cm. in length, a deep purple in colour. The insect will crawl over the skin without doing any harm unless disturbed, irritated, or hindered by clothes. Then its body exudes an irritating blistering fluid, but the blistering does not appear for 24 hours or so by which time the fact of contact may have been forgotten. The bullae it produces are round dome-shaped, hemispherical, without any surrounding erythema. Opening to release the fluid and the application of a mild antiseptic bring about complete healing without any scarring, in 10 days. Diagnosis has to be made from bullous dermatoses such as pemphigus dermatitis herpetiformis dermatitis venenata and inflammatory bullae from thermal or chemical agents.

H. Harold Scott.

#### LABORATORY PROCEDURES.

DE BURGH, P. M. Notes on Field's Stain. *Med J Australia* 1946 Apr 20 v 1 No. 16 544-5.

The author of this paper refers to some of the factors involved in the success or failure of Field's stain to produce good staining of the malaria parasite principally in achieving a red chromatin dot and blue cytoplasm.

He discussed the drawbacks in the use of preparing modifications of Field's Solution 1 and describes a modification of McNeal's acid oxidation method used by LILLIE in preparing Giemsa stain which was found satisfactory in preparing Field's first solution [this *Bulletin* 1945 v 42 414 1944 v 41 74]

DE BURGH also found erythrosin slightly preferable to eosin in Solution 2. He discusses the action of Field's stain at length and draws particular attention to the fact that when the final layer of haemoglobin left in the blood-film becomes too thick the chromatin appears blue-black. The success or failure of the stain depends mainly on the thickness of the film. He points out that preliminary removal of haemoglobin can be done in a variety of fluids none of which has any real advantage over distilled water. He describes a modification of technique which whilst it involves little increase in staining time extends the range of thickness of the films over which good staining may be obtained.

The paper contains a wealth of technical detail and in order to appreciate its considerable practical value it should be read in the original

H J O D Burke-Gaffney

RATCLIFFE A. W. A Note on Staining Plasmodia. *Science* 1946 May 17 630-31

The author suggests that our conception of plasmodial staining reactions may be incomplete

(1) Blood infected with *P. vivax* (produced clinical and typical smear positive malaria upon therapeutic inoculation) smeared and stained with Wright's stain failed to reveal any parasites

(2) Similar blood which showed numerous parasites in fresh unstained blood failed to reveal any parasites in stained smears

(3) Smears of blood with numerous parasites (*P. vivax*) which stained readily when first smeared could not after transportation (Texas to Indiana) be stained to show organisms of diagnostic acceptability

The author suggests that the solution of the problem of staining these organisms might be helpful in the ancient and recurring problem of smear-negative patients progressing to necropsy demonstration of plasmodia.

The pH of the buffer, age of smear and brand of stain are important factors which determine the quality of the result. Old smears require a lower pH and longer staining time, and alkaline buffer produces a dark [blue] smear while an acid buffer produces a red smear. The author's chief problem was failure to obtain (red) staining of the chromatin. Despite the red cast with acid buffers it was the blue which seemed to stain the nuclei of the leucocytes rather than the azure components of the stain. It is recommended that azure staining of the chromatin is improved by using alkali as a preliminary bath rather than as a medium for the stain and sodium carbonate and ammonium hydroxide were found to be satisfactory. Fresh smears may be given brief exposure to pH 8-9 after fixation and old smears to a stronger alkali, but the exact concentration or time has not yet been determined? By bathing old films in strong alkali and subsequently staining for 24 hours in Giemsa or Wright's stain satisfactory results can be produced. The possibility of shortening the period of staining by adding a penetrant such as Tergitol 7 is being investigated.

[It is well known that old unstained films are extremely difficult to stain satisfactorily. The blood corpuscles become very hard and fixation is unnecessary even when watery stains (Giemsa) are used. Such films stain a deep blue. The reviewer has found that temperature is an important factor - old films kept at 50°F stain better than do similar films kept at 80° or 90°F]

P G Shute

CHEMLOCK, R. L. & MULLER H. E. Use of Wetting Agents in Histological Fixatives. *Science* 1946 June 21 731-2.

On the grounds that the speed of penetration of a tissue fixative probably enhances its quality the authors carried out a series of experiments in which three wetting-agents were added to carefully prepared solutions of nine different standard fixing solutions. Sheep cerebrums and human liver were found to be useful test tissues and pieces of these one inch square, were placed in 250 cc. of each of the nine fixatives for 24 hours. They were then sectioned and the degree of penetration estimated grossly by the use of colouring agents. The preparations were then carefully studied microscopically. The fixative solutions employed were Zenker's Carnoy's Helly's, Bouin's Allen's, Gilson's, Orth's Vandegrift's and 10 per cent formalin. Each was modified by the addition of three aliphatic substances known to have the quality of decreasing surface tension. The aliphatics used were Tergitol-7 Tergitol-4 and Tergitol-OS. These were all used in the ratio of three drops to 100 cc. of fixative. The authors found no correlation between the various fixatives their pH component ingredients or supplementary Tergitol and the degree of penetration or the quality of fixation staining and shrinkage. They did find however that in the case of Allen's, Orth's, Vandegrift's and Zenker's fluids and also 10 per cent formalin, Tergitol-4 improved fixation and staining. Tergitol-OS produced a similar result when added to Zenker's fluid.

All other combinations of fixatives and detergents showed either no improvement or a decrease in the quality of fixation and staining.

H J O D Burke-Gaffney

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## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

INDIA. Annual Report of the Public Health Commissioner with the Government of India for 1943 and 1944 [BOZMAN C. A.]. 39 pp 1 folding map 1946 Delhi Manager of Publications. [As 8 or 9d.]

Like its predecessor this is a combined and curtailed report of health conditions in India during two years. In a pamphlet of 39 pages it is obviously impossible to deal with the subject in an adequate manner and in view of the extreme gravity of the health situation in India there is an urgent need for a comprehensive survey of recent developments in the public health field for the purpose of forming a true appreciation of the present position and a reliable forecast for the future.

The Report of the Health Survey and Development Committee set up by the Government of India in October 1943 to study the organization of health services in India covers part of the ground and among the recommendations contained in the report great emphasis is laid on the need for a special department under a Registrar General of Vital and Population Statistics, "to work independently of the Central Health Department but in close co-operation with it" to study vital statistics for the whole country and to "publish an annual report on the population of India, incorporating such information as is available regarding existing conditions and possible trends for the future. A similar organization for each province is recommended.

Reference to this matter has been prompted by the following statements in the first page of the present report. "Famine is of itself not a problem for health administrators since its occurrence is primarily dependent on the total

quantity of food available and facilities for its distribution. Health administrators are however vitally interested in any condition of famine since unfortunately such is invariably associated with the appearance of epidemic diseases due to causes other than mere lack of food. These remarks illustrate very clearly the radical defect that exists in the public health organizations of most countries of the world. Health depends not only on the control of infection but also on the control of the equally important preventable diseases caused by inadequate nourishment so that although health workers have not been provided with the means of controlling malnutrition they ought frankly to insist that all their efforts to prevent infectious disease must be fruitless unless nutritional disease is kept under control.

The number of deaths from famine in Bengal during the year ending April 9-44 is estimated at over one million. In Madras Presidency during the same period the deaths were 176 827 in excess of the average for the previous five years and in the smaller province of Orissa the excess deaths were 52 146. The birth rate for British India has continued to fall it was 25 13 in 1944. The causes of the progressive decline during the past five years need very careful consideration and this matter is said to be receiving the attention that its importance demands.

Cholera vaccines were used on a very large scale in some provinces nearly 19 million inoculations were performed in Bengal in 1944 and in Madras there were more than 8 millions in 1943. Cholera phage was still being intensively used in Bihar in 1943 in addition to inoculation.

Few statistics are given to show the prevalence of the chief diseases but among the general statements it is interesting to note that compulsory inoculation against plague was enforced in certain areas of the Punjab and that in 1944 the Government of the United Provinces issued orders that all major irrigation and hydro-electric projects and all drainage schemes should be scrutinized by the Public Health Department before completion.

A welcome note of optimism is sounded in connexion with kala azar of which it is stated that it might easily be a considerable public health problem in the areas that it attacks but that it can be said confidently to be now being kept in check, through systematic treatment which fortunately is also an effective method of control.

More than half of the report deals in general terms with the activities of the central and provincial health departments medical research and the work of the voluntary organizations.

VAN HOOF L. *Pathology of Belgian Congo during the War* *Epidemiological Information Bull* (UNRRA Health Division) Washington, D.C. 1946  
June, 15 v 2 No 11 459-63 *John W D Megaw*

SCOTT J A. *Health Problems of the Amazon Valley* *Texas Reports on Biol & Med*  
1946 v 4 No 2, 245-59 1 map

PASCALE H. *O clima e a doença.* [Climate and Disease.] *Arquivos de Hig e Saúde Pública* São Paulo  
[15 refs] English summary 1945 Sept v 10 No 25 7-30 5 graphs

General remarks on the factors which go to make up climate and a discussion of the ways in which they influence the individual the vector and the multiplication of the *maleres morbi*. Charts are reproduced which sacrifice clarity for presenting too much on a page for example a single chart is used for demonstrating the seasonal variations over 15 years of eight different diseases.



—measles whooping-cough diphtheria smallpox scarlet fever mumps meningitis and anterior poliomyelitis in Alabama and Mississippi and another for Massachusetts and Connecticut. [It will be seen that the application is very limited and therefore of interest to few. The whole is too condensed for a more detailed abstract and those sufficiently interested should consult the original.]

H. Harold Scott

HERMITTE L. C. D. Venomous Marine Molluscs of the Genus *Conus*. *Trans Roy Soc Trop Med & Hyg* 1946 June v 39 No 6 485-512, 33 figs. on 5 pls. Numerous refs.]

This is an article of great importance and value in closing a serious hiatus in tropical medicine—our lack of knowledge of poisonous marine molluscs. The author deals with stings by species of *Conus* stings which are always painful often serious and sometimes fatal. A finely reproduced plate illustrates five species known to sting man and in an appendix is a list of reported cases of each. *Conus aulicus* *C. testis* (two fatal cases among these) *C. mar-scorus* *C. tulipa* and *C. geographus* (three fatal cases).

Dr. Hermitte gives a detailed account of a case under his own observation in the Seychelles in 1932, the first to be reported as occurring in the Indian ocean up to then all had been reported from the Western Pacific. A man 32 years of age picked up a specimen of *C. geographus* and was cleaning it when he felt a sharp sting. Turning it over he saw a fine sharp needle (a radular tooth) being retracted.

"The burning sensation soon gave rise to numbness, and within a few minutes he felt his left arm tingling and gradually becoming numb. Then, feeling his head getting queer he wisely decided to regain the shore and go home. I have used the word wisely because within an hour the whole of his body was numb his sight was impaired, he had marked dizziness and nausea, he became completely paralyzed and could not move his limbs or sit up and speech was difficult. Had this occurred while he was still in the water he might well have lost his life by drowning.

After 5 or 6 hours he began to improve a little and asked to be taken to my surgery at Mont Fleuri on the main island of Mahé 3 miles distant across the lagoon.

"The accident had occurred at 9 a.m. and he was brought by pirogue (canoe) to my surgery at 6 p.m. having been carried to and from the boat in a long chair. He was still giddy and unable to stand with a feeling of general weakness in all four limbs.

On examination there was nothing to see at the site of the sting and there were no signs of hypersensitiveness such as urticaria. His knee reflexes could not be elicited but his pupils reacted normally to light and to accommodation. The pulse rate and respiration were normal there had been no respiratory difficulty at any time or any rise of temperature as far as he could tell. When examined his temperature was normal.

"These were obviously symptoms of some form of neuro-toxic poisoning. This poison paralyzes the centres of voluntary movement thus differing from the poisoning of stinging fishes which cause tetanus-like symptoms.

The author dissected specimens of the mollusc and the stages of dissection are described in minute detail and clearly shown by illustrations which will prove of much help to others desiring to carry out research into this question. With a view to finding out the nature of the poison he obtained more specimens but on their reaching England the poison had disappeared, or at least was no longer active (the specimens had been kept in alcohol). This research will probably therefore have to be carried out in the tropics on the spot. The

source of the poison seems to be the coiled tube previously regarded as the duct of the Gland of Leiblin (which is not a gland at all) Appended to the article is a list of 30-40 species of *Coxius* recorded from the Seychelles.

H. Harold Scott.

## BOOK REVIEWS

**JENSENIUS Hans** *Results of Experimental Resections of the Small Intestine on Dogs. (Experimental Enteroprival Sprue.)* [Translated from Danish by Hans ANDERSEN M.D.] 275 pp 42 charts & 69 figs. on 35 pls. 1945 Copenhagen Arnold Busck Nyt Nordisk Forlag & London H K Lewis & Co Ltd 136 Gower Street

This investigation was primarily designed to elucidate the pathogenesis of pernicious anaemia. At the time of the publication of Castle's researches attention was devoted to the stomach but since 1938 when preparations of the small intestine were found to possess an anti pernicious-anaemia effect investigations on the effects of resection of this portion of the gastro-intestinal tract were also made but it was found that resection failed to produce pernicious anaemia.

The main purpose of this very thorough piece of experimental research has been to throw additional light on a symptom-complex resulting from extensive resection of the small intestine including changes in the blood picture in the absorption of intestinal contents and in the central nervous system. The relation of the symptom-complex to the clinical picture in man especially in sprue was studied with special reference to pathogenesis.

*Previous clinical and experimental investigations*—Most investigations appear to have been concerned with the extent of resection of the small intestine compatible with maintenance of life. This has varied from one-third to nearly the entire length, but most writers regard it as about two-thirds. On the whole children or young adults withstand this mutilation better than persons of more advanced age much depends upon the pathological condition of the bowel.

There are three possible ways in which one may try to compensate for the loss of a large portion of the small intestine—

- (1) The diet may be increased in amount especially in its caloric content
- (2) It may be rendered more absorbable, poor in fat but rich in carbohydrate
- (3) From experimental studies it appears that the unresected portion undergoes compensatory hypertrophy with resulting increase in function. Such a result has not been proved to occur in the rest of the digestive tract, i.e. the stomach and colon. Physiological studies show that the capacity for fat absorption is greater in the distal than in the proximal portion of the small intestine, which suggests that the distal portion is more essential for the maintenance of life than the proximal

*The author's investigations*—The animals used in these experiments have been fairly big pups about 3-4 months old. The experimental material consisted of 25 completed experiments 15 with distal & 5 with proximal resection 4 with short-circuiting of the distal part of the small intestine and 1 with distal resection of small intestine and resection of half of the colon. In all the operation involved two-thirds of the small intestine and in three instances only with distal resection was  $\frac{1}{3}$  of the gut removed. Measurements must be taken at the time of operation otherwise owing to contraction, quite different values are obtained. All animals submitted to distal resection died.

provoke experiments with distal short-circuiting of the small intestine approximate those with distal resection.

The clinical picture particularly after distal resection of the small intestine shows many resemblances to that observed after stomach operations but differs in the relative inconspicuousness of the skin changes and achylia in fact the clinical picture is more closely allied to sprue than to pellagra.

P. Manson-Bahr

DE WILDFMAN E. [Directeur honoraire du Jardin botanique de l'Etat etc.]  
A propos de médicaments antilépreux d'origine végétale. IV. Des *Strophanthus* et de leur utilisation en médecine. [An Account of Anti leprotic Drugs of Vegetal Origin. IV. The Use of Species of *Strophanthus* in Medicine.]  
Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales.  
Mémoires (Collection in-8°) 1946 v. 15 No. 4 70 pp.

No. IV of this series of monographs gives a comprehensive account of what is known of the numerous species of *Strophanthus* in regard to the chemical constituents and their use in medicine. This genus includes 62 species 21 of which are found in the Belgian Congo whose distribution in that area is recorded. The chemical constitution of the active ingredients varies considerably both in detail and in the quantities found in different species. Only the following three have been extensively investigated, and as the strophanthins found in them differ materially in their solubilities and activities, and as different species are recognized as official in various countries, it is necessary to add the initial of the species of plant from which each is derived when dealing with their use in medicine. Thus *Strophanthus gratus* yields strophanthin-G which is official in Germany, France and the United States. *S. hispidus* yields strophanthin-H as used in a number of European and American countries and *S. kowe* provides strophanthin-K which is used in England and many other countries. Strophanthin K is 30 times as soluble as strophanthin-G and is less toxic it has been, therefore, much used for intravenous injection in Germany as it is excreted within 24 hours (against two days in the case of strophanthin-G) and is therefore less cumulative and toxic than the latter.

The alkaloids and glucosides are found in the greatest strength in the seeds but are also present in the roots and young bark. Their value in cardiac diseases, and as diuretics is well known. Other diseases in which information is given of the use of preparations from these plants, by the indigenous peoples of Africa and others include leprosy tetanus whooping cough, asthma, angina pectoris they are used as anaesthetics in eye and ear affections, for venereal diseases vermin in the head, rheumatism, and especially for poisoned arrows, for which last purpose they were formerly cultivated in West Africa. Their use in leprosy by the Ibos (according to the late Dr. Oberdoerffer) was in the form of a decoction of roots or young bark, but no evidence is recorded in this book on any results of this treatment. This work with its numerous references to the literature of strophanthins will be of great value to those interested in this important class of remedies.

L. Rogers

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## ANTI RABIES TREATMENT

A DISCUSSION OF ITS VALUE IN THE LIGHT OF RECENT EXPERIMENTAL WORK.

By A J RHODES M.D. F.R.C.P.E.D

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(University of London)**Introduction*

Anti rabies treatment was introduced into human medicine by Louis Pasteur and his associates in Paris in 1885. Pasteur had found that the common rabies virus of the natural disease in dogs or street virus when passaged intracranially in rabbits ultimately became fixed in its properties—*virus fixe* or fixed virus. He further showed that fixed virus could be attenuated in virulence by drying an infected rabbit cord in a desiccating jar. The longer the cord was left to dry the less became the infectivity. Using cords of gradually increasing virulence Pasteur was able to treat dogs so that they withstood a subsequent test inoculation of virulent virus (PASTEUR CHAMBERLAND and ROUX 1884). Encouraged by the results in dogs Pasteur decided to try the treatment in human beings. The first case treated was a success as the patient badly bitten developed no signs of rabies (PASTEUR 1885). The treatment was at once made available in Paris and by 1888 nearly 2,500 people had been treated there (PASTEUR 1888). Pasteur's method was quickly adopted in all parts of the world, either in its original form, or after substantial modification. The most important modification was the use of chemical chiefly phenolized vaccines containing inactivated virus.

For the past 50 years or more the orthodox treatment of persons bitten by suspected rabid animals has been a course of anti rabies vaccine. It is accordingly very difficult to obtain control figures that can be used in assessing the value of anti rabies treatment.

Of recent years a considerable amount of experimental work has been performed on active immunization and it has been learnt that it is difficult to prevent rabies in experimentally infected animals if the vaccine is given after infection. It has also been shown by Webster and other American workers that a number of phenolized vaccines available for veterinary and human use have been devoid of immunizing activity (see below). For these and other reasons there has been a growing feeling that anti-rabies treatment of man as at present practised may not be as effective as it was originally believed to be. It may be said in general that French workers are convinced of the value of treatment either with attenuated or chemical vaccines. Many British and

American workers on the other hand are somewhat sceptical. A critical review on the value of anti-rabies treatment published by WEBSTER (1939 a) has brought the subject very much into prominence.

It is my object to discuss the scientific basis on which anti-rabies treatment rests with particular reference to recent experimental work. At the same time I shall try to explain some of the variable factors that make the evaluation of this treatment in human beings so difficult. Fuller references to many of the points raised will be found in an earlier publication (VAN ROOYEN and RHODES 1940).

### *Some Features of Rabic Infection in Man*

*Some properties of the rabies virus*—Rabies as it occurs in nature is caused by an agent known as *virus de rage de rue* or street virus. This agent is commonly accepted as being a filterable virus although it is regarded by some as a protozoon, on account of the resemblance of the characteristic Negri inclusion body to certain protozoa. Street virus can be transmitted to laboratory animals such as monkeys rabbits guinea-pigs and mice, by peripheral or intracranial injection. After peripheral injection e.g. in the muscles virus remains viable locally for at least 4 days invades nerve fibres within 24-48 hours and spreads to the cord along these channels (HABEL, 1941 b). There is no evidence that the blood stream is concerned in the dissemination of the virus to any significant extent after peripheral injection. Virus has been recovered, and histological changes have been found most readily in the portion of central nervous system corresponding to the site inoculated (GOODPASTURE 1925 WEBSTER, 1937 1939 b HÄGLER and BERNKOPF 1943). Rabies infection can also be induced by direct intraneural injection of virus. Not only does street virus spread to the central nervous system centripetally after peripheral injection but it also spreads out centrifugally therefrom along other nerves. By the end of the incubation period virus is probably widely disseminated throughout the peripheral and central nervous systems. The term *septicaemia* is applied to this essential neurotropic property.

After intracranial inoculation of street virus in for example rabbits or guinea-pigs symptoms of rabic infection develop in about 14-20 days. If the brain of such an animal is passed intracranially in series it will be found that the incubation period becomes progressively shorter and eventually "fixed" at about 5-8 days. The virus is now known as *virus fixe* or fixed virus, and is remarkably stable in its properties. Negri inclusion bodies are not normally formed by fixed virus.

It is probable that strains of street virus may vary considerably in virulence for man. Thus certain strains found particularly in wolves and known as *renforcé* strains produce paralysis in rabbits on intracranial inoculation after a shorter incubation period than usual. Such strains may become fixed after only a few intracranial passages. At the other end of the scale is the *oulofalo* virus of indigenous African mad-dog disease. These strains are of definitely reduced virulence for man. Although it has been suggested that *renforcé* strains are associated with unusually virulent infections, failing to respond to anti-rabies treatment the position does not seem to be sufficiently clear for a definite statement to be made on this point (PROCA and BONES, 1940).

Fixed virus does not infect the experimental animal so readily as street virus by peripheral routes and does not show *septicaemia* to the same degree. Fixed virus is probably of considerably reduced virulence for man and may even be non-pathogenic on subcutaneous inoculation, unless large quantities are injected.

Observations that have been made on the antigenic structure of rabies viruses do not point to any marked differences between strains (see HAVENS and

MAYFIELD 1933) It would be in keeping however with the newer knowledge of viruses if future work showed strains to differ considerably one from another. In recent years such antigenic variations have been found in strains of poliomyelitis and influenza viruses for example.

*Sources and modes of human infection with rabies*—Rabies exists in nature as an enzootic in dogs, wolves, jackals, mongooses and other animals and may be transmitted to man as it were accidentally by the bite of a rabid animal. The majority of bites treated in anti rabies institutes throughout the world are inflicted by dogs. In India about a third of all bites are inflicted by jackals and in parts of Europe wolf bites are relatively frequent.

Dogs especially in tropical climates are liable to bite human beings apart altogether from rabies by no means all dog bites therefore even in countries where rabies is endemic are inflicted by rabid animals. It is thought that only about 50 per cent of rabid dogs actually excrete rabies virus in their saliva (WEBSTER 1942) presumably therefore only one in every two rabid dogs is actually a source of danger to persons it may bite. Wolves and jackals are said seldom to bite man unless rabid.

On occasions rabies may follow scratches or licks of rabid animals but this must be regarded as a great rarity. It is likewise most unusual to contract rabies from animals other than the four already mentioned. [This survey does not include rabies in Trinidad where the virus has been shown to be transmitted by species of vampire bat.]

*Pathogenesis of human rabies*—After the bite of a rabid animal virus probably remains localized in the wound for 24–48 hours and then invades nerve fibres. Virus may persist locally as it has been isolated from the scar (PACE 1903). Virus has been recovered from nerve fibres in man on various occasions (PASTEUR *et al* 1884 BARDACH 1888 ROUX 1888 1889 PACE 1903) and histological changes have been found in the nerves of the bitten limb and corresponding spinal ganglia (MARINESCO and DRAGANESCO 1932). *Septicæmia* occurs in man as in animals and virus has been isolated from nerves other than those of the bitten limb histological changes may also occur (MANOUÉLLIAN 1936).

All the evidence points to the virus being disseminated in the body by nerve tracts and not to any significant extent by blood or lymph. It is held by many that the length of the incubation period is related to the distance of the wound from the spinal cord or medulla i.e. to the length of the nerve paths to be travelled by the street virus. For instance WEBSTER (1944) gives the following average incubation periods—

bites on head, face and neck—30 days

bites on upper extremity—40 days

bites on lower extremity—60 days

JOHNSON (1943) however maintains that more important factors are the amount of virus inoculated into the wound and the type of tissue bitten. The shortness of the incubation period after wounds on the head, face and neck is ascribed to the frequently severe nature of these bites and the abundance of nerve filaments available to be invaded.

It is not known how long street virus takes to reach the central nervous system from a peripherally situated bite. It is presumably present in the central nervous system for several days before the onset of symptoms and during this time centrifugal spread along nerves is taking place.

In certain circumstances it would appear that rabies virus can remain latent in the body without causing symptoms especially if anti-rabies treatment has been applied for rabies has developed after an incubation period of as long as 3 years (IYENGAR, 1935). In some cases that develop unusually late the onset of the disease may be provoked by an emotional shock (REMLINGER, 1946).

The minimal amount of virus required to infect man is not known, nor is it known if sub-infective doses inoculated in a wound in untreated persons can invade nerve paths and set up an asymptomatic infection. There is some evidence that man has an innate resistance to rabies, at any rate to the common type of canine street virus perhaps because the disease is normally spread from dog to dog, and the agent is not well adapted to invasion of human tissues.

*Mortality from rabies in untreated persons.*—Once rabic symptoms develop the disease is invariably fatal but only a comparatively small percentage of persons bitten by rabid animals actually develop rabies. It is extremely difficult to estimate scientifically the chances of dying of rabies following the bite of a rabid animal. Mortality figures should be based on observations made in the groups of persons bitten by known rabid animals none of the bitten being treated in any way. All the persons in question would have to be observed for a year or more to make certain that rabies did not develop. Statistics of this type are not available. Numerous observations on groups of bitten persons untreated but selected to a greater or lesser extent suggest, however that an average mortality figure is from 5 to 15 per cent this being modified by a number of factors. Thus the mortality is higher in wolf bites probably over 60 per cent especially if situated on the face. The mortality is higher in deep than in superficial wounds, in wounds on the face in multiple wounds and in wounds inflicted through bare skin (see HARVEY and MCKENDRICK, 1923). In fact the mortality from rabies in untreated persons is directly proportional to the amount of virus deposited in the wound by the biting animal and to the degree of trauma inflicted on the tissues.

*Cauterization of bites of rabid animals.*—The orthodox first-aid treatment of bites inflicted by rabid animals is cauterization, by the thermocautery or by strong agents such as corrosive acids. Experimental work on guinea-pigs infected by intramuscular injection has shown that application of iodine or washing with soft soap and water is as effective and does not cause scarring (STRAUGHNESS and ZIEHL 1943). Experimental observations suggest that cauterization may itself protect against rabies, even if applied up to 24 hours later (CABOT 1889 POOR 1911 ROSENBAUM 1935). Even if promptly applied however it may fail to protect some animals (BARES and TALASESCU 1894). Presumably in such cases the cauterizing agent fails to reach virus living in pockets.

HARVEY and MCKENDRICK (1923) reported that efficient cauterization reduced the chances of developing the disease in the proportion of 4 : 3. MACKIE (1928) found it advantageous to open up wounds and wash with acriflavine. I have tried but without success, to obtain more recent figures from Pasteur Institutes relating to the value of cauterization. From what has been said it will be evident, nevertheless that cauterization has a definite protective effect. This is one of the many factors that complicate the evaluation of anti-rabies treatment: as both treatments are frequently given together.

#### *Experimental Observations on Active Immunity in Rabies.*

Animals can be immunized by anti-rabies vaccines given prior to infection. Under certain circumstances they can be protected from rabies by injections of vaccine given after infection.

*Type of vaccine.*—Numerous preparations have been used to induce active immunity in animals the more important are as follows:—

(a) Living or attenuated *virus fixe* prepared as in Pasteur's or Hoegye's method, can be used, and is an effective immunizing agent, but is not widely employed owing to the risk of death if large quantities are given. It was found that fresh living *virus fixe* used as an adjunct to the phenolized virus immunized

dogs more effectively than any other method (SHORTT *et al* 1934-5) WEBSTER (1939 *b*) using mice also found live virus vaccines to be effective immunizing agents.

(b) Chemical vaccines of various types have been much used. Phenol, chloroform, ether and formalin inactivate rabies virus if left in contact for a sufficient time and if used in adequate concentration. The process of inactivation is gradual and chemical vaccines are sometimes used at a stage when virulent virus can still be detected by animal inoculation. More usually, however, chemical vaccines are used when the virus appears to be destroyed and no sign of infection can be detected in inoculated animals. We know so little about the true biological nature of living rabies virus that it is perhaps unwise to assert that these vaccines contain 'dead' virus. All that can be said is that with products such as Semple's phenolized vaccine, tests for infectivity consistently prove negative. Whether a killed chemical vaccine contains virus in a form that may be reactivated *in vitro* is not known. It is perhaps more appropriate to refer to chemical vaccines as containing 'inactivated' virus.

Provided that the vaccine contains a sufficient quantity of virus material and that the strain is of high immunizing potency (see below) a satisfactory state of resistance can be induced in laboratory animals to a peripheral test dose and even to an intracranial injection. Injections must be given repeatedly and in large doses—for example a monkey may require as much vaccine as is used for a human being. WEBSTER (1939 *b*) using a phenolized and a chloroformized vaccine found that mice required a dose approximately five times as great as that advocated per gramme of body weight for man. There is some evidence that chloroformized vaccines are better immunizing agents than phenolized products. Etherized and formalized vaccines are also used.

(c) Virus grown in tissue culture can be used in its live state, formalized or attenuated by ultra violet light (HODES *et al* 1937-1940; WEBSTER, 1937-1938; KLIGLER and BERNKOPF 1938-1941; WEBSTER and CASALS 1941).

(d) The principle of attenuation by exposure to ultra violet light has also been extended to infected brain tissue (SANKARAN and BEER 1934-5; WEBSTER and CASALS 1940 *a* 1941 1942 *a* *b*; LEVINSON *et al* 1944). It is almost certain that the virus is not completely destroyed in these vaccines as they become less effective if inactivated for too long. Such vaccines are the most potent yet produced and mice have been protected with them against 10 000 lethal ( $LD_{50}$ ) doses of virus whereas a chloroformized vaccine protected against only 1 000 lethal doses (WEBSTER and CASALS 1942 *a*).

(e) Virus inactivated by the photodynamic action of methylene blue is antigenic but probably only if some live virus remains in the preparation (GALLOWAY 1934; SHORTT and BROOKS 1933-4 1934-5).

*The strains of virus fixe used in vaccine production*—Anti rabies vaccines are usually prepared from the classical Pasteur strain of *virus fixe* of which a number of 'off-shoots' are maintained in various institutes. It was found that the Pasteur strain was a more efficient antigen than *virus fixe* prepared from strains isolated in India (CUNNINGHAM *et al* 1933; SHORTT *et al* 1934-1937).

The most important recent work in this connexion is that of HABEL (1940 *b*) who examined 31 strains of *virus fixe* of which 25 were derived from the original Pasteur strain. He made the important observation that these strains differed considerably in their ability to immunize mice. He suggested that a high immunizing potency against a heterologous test virus is not an inherent characteristic of a strain but can be altered during transfer. HAMPTIL and ROBERTS (1942) made similar observations and showed that substrains of the



same strain varied considerably, and might afford only slight protection even against the homologous virus.

With any given strain of virus *fixe* the greater the amount of virus material the greater is the immunizing capacity of the vaccine. It is therefore desirable to ensure the maximum content of virus in the brain tissue used in the vaccine, and for this purpose HABEL (1941 a) recommends that animals be inoculated with dilute rather than concentrated suspensions of passage brain.

Laboratories preparing anti-rabies vaccines should periodically test the properties of their strain of virus along the following lines (HABEL, 1940 b) specificity should be checked by a neutralization test with antiserum samples should be removed during the process of treatment with chemicals and tested for virulence in mice attenuated vaccines should be similarly tested mice should be immunized with the vaccine as ready for issue and tested by intra-cerebral injection.

*Technical methods in testing active immunity*—In tests for the immunizing potency of vaccines it is customary to inject the subsequent test or "challenge" dose of live virus by a rate that kills as nearly as possible all the control unvaccinated animals. Unless this dose is given intracerebrally or intraocularly it is often difficult to secure infection of more than 50-75 per cent. of controls.

Various workers using relatively ineffective vaccines, have experienced difficulty in immunizing animals sufficiently to withstand intracerebral or intraocular injections of test virus, although a peripheral injection might be resisted (see WEBSTER, 1939 a 1942). Live vaccines and the newer irradiated and chloroformized vaccines will definitely protect against a subsequent intra-cranial test dose.

In all tests of this type an accurately titrated amount of virus must be used for estimating both the immunizing dose and the "challenge dose" for this purpose it is usual to inject mice intracerebrally with falling serial tenfold dilutions using at least 6 mice per dilution. The  $LD_{50}$  or 50 per cent. mortality endpoint, which is a convenient measure of the potency of the inoculum, is then calculated. The method introduced by RIXED and MUEHLEN (1938) gives additional accuracy to this calculation.

Vaccines are now usually assayed by a mouse test such as that introduced by WEBSTER (1939 b 1940 1941) which is carried out as follows. The vaccine to be assayed is diluted 1/10 and 1/8th of the stated dose is used (representing 1/80th). A total of 32 three-week-old mice are needed. In the case of canine vaccines one dose is given intraperitoneally to each of 16 of the mice. In the case of vaccines intended for human use, the mice are given 3 to 6 injections. Three weeks after the first injection of vaccine the test and the 16 control mice are each divided into four lots and injected intracerebrally with 1 10 100 and 1,000 lethal ( $LD_{50}$ ) doses. To detect a weak or immunizing effect the challenge dose can be given intramuscularly from 2 to 32 lethal doses being used. Both test and control mice are examined for 60 days.

Somewhat similar tests have been introduced by WYCKOFF (1940-1 WYCKOFF and BECK, 1940 WYCKOFF and TEXAR, 1941) and HABEL (1940 a) HABEL considered that the minimum requirement of a vaccine tested by his method was that it should protect against at least 1 000 lethal doses calculated by the 50 per cent. end-point method.

WEBSTER regarded the mouse immunity test as of considerable value in indicating the immunizing efficiency of anti-rabies vaccines, and it certainly appears to be by far the most practical and at the same time accurate, method available. REMLINGER and BAILLY (1943) however question whether mice are really suitable for such tests and suggest that they are unduly susceptible to rabid infection.

Dogs have also been used extensively in testing anti rabies vaccines and in general, a vaccine proved potent by mouse test proves effective when tested in dogs (JOHNSON and LEACH 1940 1942 LEACH and JOHNSON 1940 1942 WEBSTER and CASALS 1940 b)

It may be argued that some of these tests are too severe and in many ways the most valuable method of testing the immunizing potency of vaccines is to attempt to imitate what happens when they are used in human treatment. Thus monkeys may be challenged by street virus injected intramuscularly or, better still saliva from rabid dogs could be employed.

WEBSTER (1939 b 1940) tested a large number of commercially prepared vaccines available for sale in the U.S.A. for use in human anti-rabies treatment and for the prophylactic immunization of dogs. With the exception of one product he found that the phenolized vaccines failed to immunize mice against a subsequent intracerebral challenge dose of even one lethal dose. chloroformized preparations were somewhat more effective. With dogs chloroformized vaccines were found to give protection if the challenge dose was given intramuscularly, the phenolized vaccines studied in this work being valueless (see also WEBSTER and CASALS 1940 b 1942 a LEACH and JOHNSON 1940)

A considerable amount of work has been carried out on the mass prophylactic vaccination of dogs as a means of controlling rabies and it has been customary to give only one injection. The observations of Webster just quoted showed however that the bulk of canine vaccines sold for the purpose were quite unable to confer a significant degree of immunity after a single injection. If large or repeated doses of potent phenolized or chloroformized vaccines are used a high degree of immunity can be acquired and the irradiated type of vaccine is even more potent.

*Anti-rabies treatment of experimentally infected animals*—As has been seen above, it is perfectly possible to immunize animals by injections of potent vaccines containing live or inactivated virus given prior to the test dose of living virus. Immunity of this type has little direct bearing on anti-rabies treatment of man however where the course of vaccine has to be administered after the infection has been initiated. Accordingly a number of workers have tried to prevent rabies from developing in animals infected by peripheral routes by giving courses of anti rabies vaccine after infection and in general, have found it difficult to achieve protection (for references see WEBSTER 1939 a 1942)

For example extensive work, chiefly with monkeys was carried out over a period of years in India using chemical vaccines. Although some degree of protection was shown the results were disappointing as it was not possible to protect as many as 50 per cent of animals, if the treatment was given after infection was initiated (CUNNINGHAM and MALONE 1930 CUNNINGHAM *et al* 1933 SHORTT *et al* 1934 1934-5 COVELL *et al* 1936-7)

Certain workers have been more successful. FERMI (1908) for instance treated rats with large doses of vaccine after infection and secured a significant degree of protection. More recently HABEL (1940 a) working with guinea pigs infected intramuscularly was able to protect 16/27 by a series of 21 daily injections of 0.5 cc. phenolized vaccine. 4/5 controls developed rabies. It may be noted that the dose of vaccine used was very large as compared with the dose recommended for human treatment. In another series of experiments mice infected intramuscularly with street virus were not protected by subsequent injections of phenolized virus although chloroformized vaccines occasionally protected when five doses of an irradiated vaccine were given rabies was prevented in most instances (WEBSTER 1939 b WEBSTER and CASALS 1942 a)

It may be concluded therefore that it is difficult to protect laboratory animals by anti-rabies treatment given after infection. Large doses of chloroformized phenolized and particularly the potent irradiated vaccine may, however, secure protection in the smaller laboratory animals. A powerfully protective effect of vaccines in infected monkeys has yet to be shown.

*Serum therapy in experimental rabies*—Virus-neutralizing antibodies develop in the blood of infected animals and human beings. Powerfully rabidicidal sera can be produced by hyperimmunization of animals for instance in sheep or rabbits by inoculation of phenolized virus followed by the living agent (SHOKTT *et al* 1934-5 HABEL, 1940 & 1945)

A number of workers have shown that rabies can be prevented in experimental animals by injections of antiserum given just before or just after injection of the virus. For example antiserum can protect mice when injected before an intracerebral test dose, and is effective even up to 4 days later (HOYT *et al.*, 1936 HOYT and GURLEY 1937-8 1938). Other recent workers have also demonstrated the protective effect of serum (*e.g.* PROCA *et al.* 1935 YEN 1942 FRIEDEMANN *et al* 1944). Special mention must be made of the observations of HABEL (1945) who worked with guinea-pigs and mice. He found that serum was most effective when given intramuscularly at the site of inoculation and immediately after the virus. The treatment of infected animals with serum gave consistently better results than vaccination alone. The best results were achieved when serum was followed by vaccine treatment 6 days after the administration of the serum.

*Mode of operation of anti-rabies treatment in experimental infections*—We have seen that courses of potent anti-rabies vaccine given before and in certain circumstances after infection can protect the experimental animal from rabid infection. What immunity mechanisms are involved? Is there a different explanation for immunity produced by live virus, by "killed" virus, and irradiated virus which is probably attenuated and not actually destroyed?

When the vaccines are given before infection there is ample time for the body to build up protective mechanisms in the ordinary way and in the active immunity acquired by this method there are probably two main mechanisms concerned. Serum virus-neutralizing antibodies presumably play some rôle, although they cannot always be detected in animals which are nevertheless resistant to infection. The beneficial effects of rabies antiserum on experimental infection presumably due to destruction of virus at the site of inoculation, should be recalled. Secondly the immune tissues appear to exert some direct virus-neutralizing effect (KUBES and GALLIA, 1944). It has been shown that when virus is introduced into the tissues of an actively immunized animal it disappears from the site of inoculation more quickly than in a normal animal and probably does not invade nerve tissue at all (HABEL, 1941 & KLIGLER and BERNKOFF 1943). The reticulo-endothelial system may also be concerned as the immune state is said to be abolished by blockade with Indian ink (LOEFFLER and SCHWENBURG 1933-4).

It is difficult to see how this more or less direct neutralization of virus by serum or tissue can play a part in the immunity acquired by post-infection treatment. The course of injections cannot stimulate the production of significant amounts of antibody for several days, and by this time the invading street virus must have progressed far along nerve tracts *en route* to the central nervous system, and be no longer accessible to circulating antibodies. Two alternative suggestions can be advanced to account for the resistance undoubtedly acquired under certain circumstances by animals subjected to anti-rabies treatment after infection—

(1) It may be assumed that the infecting virus does in fact invade and pass along nerve tracts. This process takes time and before the virus has reached

the central nervous system the course of injections of vaccine has rendered the normally susceptible nerve cells resistant to invasion. Serum antibody may play some part though probably small in this neutralization. It may neutralize any virus remaining in the wound but cannot affect that in nerve tracts. The antigen in the vaccine injected subcutaneously must be absorbed by the lymph or blood so that it can reach the nervous system ahead of the street virus. If the vaccine contains live virus, presumably some particles of virus *fixe* may invade nerve fibres and spread to the central nervous system by this route. As large quantities of vaccine are always given it is certain that the bulk of the virus must be absorbed from the site of injection by the lymph or blood stream.

The immunity according to this suggestion must be chiefly dependent upon an acquired resistance of the nerve cells.

(2) Of recent years much has been learned about a phenomenon of virus immunity known as interference. Thus it has been shown that under certain conditions the presence of one virus may interfere with and prevent the growth of a second usually closely related virus. For example mixtures of Rift Valley fever and yellow fever viruses when inoculated in the monkey did not prove so pathogenic as yellow fever virus alone (FINDLAY and MACCALLUM, 1937).

HENLE and HENLE have carried out important studies using influenza virus exposed to ultraviolet irradiation as an interfering agent (1944 a & b 1945 a & b). Thus in experiments in eggs, they showed that virus almost completely inactivated by ultra violet light was capable of preventing the multiplication of active virus introduced into the same egg some hours later or a short time earlier. Although virus might be prevented from multiplication by the interfering dose it was not actually destroyed. The interfering agents in these experiments were found to be the elementary bodies themselves.

For interference to occur in virus infections the interfering agent must, apparently, be living or else attenuated as by ultraviolet light. It is improbable that a true interfering effect can be produced by an inert dead virus.

When injections of live or irradiated vaccine are given after infection it is probable that the bulk of the fixed virus in the vaccine is absorbed into the blood and reaches the central nervous system. Here the virus particles occupy susceptible nerve cells and may produce some histological changes (see below). When the street virus ascending slowly along nerve tracts reaches the central nervous system it finds the cells it would normally infect already occupied. Hence no infection can be initiated. It is probable that the street virus is not actually destroyed by the interfering agent, and may remain latent for a period, perhaps to give rise to symptoms of rabies after a long interval.

It is difficult to see how killed particles in for example Semple's phenolized vaccine can act as interfering agents unless, as suggested above some reactivation occurs in the tissues.

In support of the suggestion that the interference phenomenon may operate is the fact that definite lesions occur in the central nervous system of animals vaccinated by the Pasteur method (NICOLAU *et al.*, 1931 CRUVEILHIER *et al.* 1935). These lesions have been attributed to a mild infection by the attenuated virus. Thus there is some cellular infiltration and satellitosis of nerve cells. Further LÉPINE and SAUTTER (1938) found nuclear inclusions in brain cells after vaccination with phenolized virus and attributed these to the presence of living virus in their vaccine.

At this point it may be of interest to refer to certain work carried out with bacteriophage which has recently been reviewed by DELBRICK (1946). Although the precise biological position of this agent is obscure it is evident that it has many properties resembling those of animal viruses. When attempts

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## SUMMARY OF RECENT ABSTRACTS \*

## IX. LEPROSY

*Epidemiology*

JONX (p. 389) contributes an interesting note on a small focus of leprosy which existed up to 1927 in Switzerland. Two groups of people were involved, and in each group there was a strong family history of the disease.

DHARMENDRA and SAMTRA (p. 738) review the results of leprosy surveys made by the latter in various parts of India. The incidence varies considerably from 0.17 to 6.64 per cent of the population in different parts; the incidence of lepromatous disease varies from 0.1 to 0.98 per cent, providing from 5 to 62 per cent of the total cases. A high total incidence is usually associated with a high incidence in children and of lepromatous cases. The proportion of infected children varies greatly. The authors make the point that in some areas patients with advanced disease are isolated in their own homes or in huts outside the villages, and that where such measures are customary a high lepromatous rate tends to be associated with a low gross incidence and a low child rate. This indicates that such measures help to control infection; the tendency should be encouraged.

In the Annual Report of the Indian Council of B.E.L.R.A. for 1944 (p. 1005) the same point is made: that a comparatively high lepromatous rate may be accompanied by low gross incidence and a low child rate in areas where some kind of isolation is practised.

In the annual report of the Madras Provincial Council of B.E.L.R.A. (p. 290) it is stated that village surveys have shown a gross incidence rate of 2.47 per cent and a child rate of 2.68 per cent; these are very high. There are great variations in the infectivity rates in different villages. A reduction in child infections has followed night segregation of infective patients in villages, by which means contact with susceptible children is reduced. It is estimated that 5 000 to 7 000 persons with leprosy are living in Madras city, of whom some 10 per cent are probably infective.

An account of leprosy in the Tehri Garhwal State, United Provinces, India, is given by SAMTRA (p. 393). A survey showed an incidence of 2 per cent, and a high proportion of cases are infective. SHAMA RAO (pp. 393-1005) reports on leprosy surveys in Hyderabad, where incidence varies from 0.24 to 0.36 per cent., and where 31 to 43 per cent. of the cases found were lepromatous.

MUIR (p. 390) has paid return visits to Antigua, St. Kitts and Nevis and Jamaica, and reports on the progress made in relation to leprosy since his first visit. These reports are primarily of local interest. VAN DER SAR (p. 391) gives an account of the history of leprosy in the Dutch West Indies.

Leprosy surveys in Bolivia have shown an incidence rate of 0.07 per cent. SUAREZ (p. 813) shows that the foci are active, stationary, or in the process of becoming extinct. Of the cases found the great majority were in males of middle age. Various measures are being taken for treatment and contact examination.

MUIR (p. 1004) has given an account of the past work of B.E.L.R.A. and outlines plans for future work in the Colonies.

*Aetiology*

DAVISON (p. 295) has found *Mycobacterium leprae* in scrapings from the nasal mucosa in cases of nerve leprosy, but only rarely in material from incision of a macule.

The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

He makes the point that smears should be stained for 20 minutes in warm fuchsin and decolourized for 20 minutes in 5 per cent sulphuric acid. If these times are reduced there is a danger that diphtheroids may retain the stain and be mistaken for *Mycobacterium leprae*. By using a triple stain ALEXANDER JACKSON (p 899) has demonstrated non acid fast forms of *Mycobacterium leprae* in nasal smears and in skin of leprosy patients. Zoogloal and spore-like forms were also apparently demonstrated.

DHARMENDRA and MUKHERJI (p 900) have failed to infect splenectomized monkeys by intraperitoneal injection of clippings from the skin of lepromatous patients. They have therefore not confirmed previous work by others who have claimed success by this method.

DE SOUZA ARAUJO (p 132) has cultivated strains of acid fast bacilli from groups of ticks of various species which had been allowed to feed on leprosy patients and which had subsequently been triturated and inoculated on to Loewenstein's medium. He considers these pigmented organisms to be *Mycobacterium leprae* and from them has prepared leprolins for use in intradermal tests. These have been compared with lepromin in a series of tests carried out by MARIANO (p 133) there was considerable difference in the results.

DE SOUZA ARAUJO (p 1006) has infected white rats by infecting them subcutaneously with emulsions of the glands of a patient with leprosy which were rich in *Mycobacterium leprae*. From some of the organs of the rats he succeeded in cultivating chromogenic acid fast organisms. He (p 1006) has also cultivated on Loewenstein medium acid fast organisms from pus taken from a fluctuating leprotic lesion of a boy. When these cultures were injected into animals they caused abscesses in the axilla, peritoneum and elsewhere but smears from the viscera were negative.

GRAU TRIANA (p 212) claims to have cultivated leprosy bacilli on modified Petraghani's medium to which at the time of sowing 10 drops of a solution of oxidase from potato with or without 10 drops of a solution of ferrous sulphate are added. The reasoning which led to this method is that in media sterilized by heat such ferments are destroyed but that the tubercle bacillus can grow because it supplies its own ferments whereas the leprosy bacillus is deficient in oxidase. The author states that colonies began to appear in 5-7 days. In a second paper GRAU TRIANA *et al* (p 213) give details of several media used on these lines.

TROUT (p 900) has cultivated an acid fast organism from lepromata on a Difco agar medium over which  $\text{CO}_2$  was passed during incubation.

IGNACIO CHALA and LLERAS RESTREPO (p 568) have studied 6 strains of acid-fast bacilli isolated from leprosy lesions in man by inoculation into animals and have made a detailed account of the lesions provoked. Complement fixation reactions were tested with certain well-known strains and in a minority of cases positive results were obtained.

### *Pathology and Clinical Findings*

PARMAKSON (p 295) has made careful histological examinations of the skin in various types of leprosy. He concludes that active skin lesions in nerve leprosy are characterized by tuberculoid changes but that these changes do not occur in lepromatous leprosy. In clinical nerve leprosy lepromatous changes are not found. If a change from one type to another occurs the typical appearances of the one disappear before those of the other arise. The Mitsuda reaction is usually negative in lepromatous leprosy and positive in nerve leprosy.

CERRUTI (p 567) made a detailed study of biopsy material taken from the nasal septa in leprosy and points out that some of the pathological changes may be found in patients who clinically appear to be normal. This kind



of examination may therefore be useful and important in early diagnosis and especially in contacts.

MESTRE MIYARES (p. 43) classifies leprosy as lepromatous, tuberculoid or non specific. The first type is infective, the second not, and the third may remain true to its form (the neural type) or may pass to either of the others.

DE SOUZA ARAUJO (p. 1010) on the other hand, thinks that the division of leprosy into lepromatous, tuberculoid and macular types is artificial and that all forms are mixed. By examining the cutaneous lymph in tuberculoid cases he has found small granules and coccobacillary forms of the organism and thinks that relapses in apparently burned-out cases are due to development of these forms.

IBARRA PEREZ and GONZALEZ PRENDES (p. 1009) note that in children separated from leprosy parents there is usually a silent interval, lasting up to 5 years before signs of leprosy appear in them. They have analysed the initial lesions seen in a large number of cases of leprosy. These were macular in 37.9 per cent, but areas of anaesthesia, infiltration of the ears, systemic disturbance with fever and rhinitis were the first signs in smaller percentages. Most of these early lesions were on uncovered parts of the skin. The authors think that the nose is not the portal of entry, but rather the portal of exit of the organisms. Examinations of the placental tissues, umbilical cord blood from the cord and from the infants themselves in a series of 16 newly born children of leprosy mothers were made by TRESPALACIOS and JOVER (p. 212) with completely negative results for leprosy bacilli.

DR SOUZA (p. 567) reports a case of leprosy in which ptosis, enophthalmia and myosis were present possibly due to leprosy. The syndrome is well known but is usually the result of other conditions.

ARGÜELLES CASALS (p. 568) describes a case in which exquisite tenderness of the finger tips and nails was present along with leprosy. He does not argue that leprosy was necessarily the cause of this condition.

DEGOTTX (p. 295) has investigated the question of the infectivity of neural leprosy in the pygmies of the Belgian Congo. On the whole he thinks that such patients are at times infective.

Changes in the euglobulin tyrosin and the albumin-globulin ratios in leprosy are attributed by ROSS (p. 297) to hepatic dysfunction and to liver damage.

#### *Leprosin. Other Tests.*

At the Leprosy Research Department, School of Tropical Medicine, Calcutta (p. 739) further research has been done by DHARMENDRA on the antigens of the leprosy bacillus and other acid-fast organisms. The acid-soluble fraction of all these is active, giving positive reactions in neural leprosy and negative reactions in lepromatous disease. The fact that one of the tested organisms (Hedrowsky's) is easily cultivated will greatly simplify the production of an antigen of value in prognosis.

BECHIELLI *et al.* (p. 800) have tested with lepromin persons (in New York) who have never been in contact with leprosy. Some positive results, both delayed and early, were given. They found that the early reactions were given in 35 of 36 tested, by people positive to tuberculin and think that infection with the tubercle bacillus may account for this result.

ROTHBERG (p. 568) produces convincing evidence to show that leprosy patients negative or weakly positive to lepromin are much more likely to develop serious reactivation of the disease than those who give strongly positive results. If this fact were appreciated, the preventive medical services could concentrate more actively on following up the negative and weak reactors, who are prone to relapses of infective type. FERNANDEZ (p. 471) makes the point that, in an infected person, a positive reaction to lepromin indicates good resistance and a

good prognosis. A negative test in such persons is an indication that careful observation is needed, and it is advisable to start treatment. prognosis should be guarded. The same author (p 297) has found that non-leprosy persons can be rendered sensitive to lepromin by intradermal injection of suspensions of *Myco leprae* or of tubercle bacilli. The early reaction to lepromin (due to the protein fraction of *Myco leprae* and to be distinguished from the late Mitsuda reaction) can be attributed to previous sensitization by leprosy or tubercle bacilli.

MOX and BASOMBRO (p 1012) have continued their work on lepromin and 2-4 dinitrochlorobenzene and now report that intradermal injection of each of these substances gives reactions which in the majority of cases are remarkably concordant. There are few cases in which they are contradictory. The injections may provide early or late reactions and these tend to be negative in lepromatous leprosy and positive in tuberculoid and non-characteristic cases.

DE SOUZA ARAUJO and MIRANDA (p 1007) found that ticks fed on leprosy patients may take up leprosy bacilli and that from these ticks acid fast organisms can be cultivated. Similar findings are recorded by DE SOUZA ARAUJO (p 1007 1008) in the case of triatomid bugs, certain mosquitoes, sandflies, simuliid flies and leeches but not in the case of *Cimex lectularius*. The same author (p 1008) has cultivated the acid fast organisms taken up by these insects and has obtained 7 cultures, one from the original patient, the remainder from ticks and triatomid bugs. He and his colleagues (p 1009) have attempted to transmit leprosy to man by the bite of infected triatomid bugs but the results were indefinite [partly, perhaps because the persons whom it was intended to infect were burned-out leprosy patients].

A somewhat similar experiment was carried out by DE OLIVEIRA CASTRO and MARIANO (p 1009) but with mosquitoes instead of bugs. After the infected mosquitoes had bitten patients with burned-out leprosy, acid fast organisms were found in the connective tissue spaces near the bite but there remains the possibility that they were there before the experiment was made.

DE SOUZA ARAUJO (p 1010) describes his method of preparing lepromin from lepromata by emulsification and addition of phenol. MARIANO (p 1010) has tested 5 of the leprolins prepared by de Souza ARAUJO, three of them were derived from cultures of acid fast organisms from ticks (see above). He compared the results of tests with these leprolins with results given by lepromin and found a considerable degree of agreement though there was some variation between the different leprolins. MIRANDA (p 1011) has done similar work with similar results. In general, these leprolins tend to give negative reactions in lepromatous cases and positive reactions in nerve leprosy.

BALAGANGADHARAN (p 739) brings evidence which supports the view that the Kahn reaction is quite often positive in leprosy in the absence of syphilis. ECKLES and ROSS (p 297) state that the Mazzini flocculation slide test though not so sensitive in leprosy as the Kolmer and Kahn tests has the advantage of greater simplicity.

### Treatment

At a Conference held at the Pretoria Leper Institution (p 292) DREWE referred to the value of rest and good food in the treatment of leprosy. DAVISON defined the criteria of cure which should be applied before patients are discharged from hospital. He also discussed the kind of leprosy institution which would be suitable for South Africa and other countries with a similar incidence of leprosy and the question of compulsory segregation of which he approves in certain conditions. MOISER showed that conjugal infection in Southern Rhodesia was low 1.57 per cent and referred to the possible transmission of the disease by cockroaches. THORNTON noted that at the institution for leprosy in the

Transkei 27.3 per cent of patients had been discharged during the past 10 years in some of these recrudescence had occurred.

No benefit from the use of pooled plasma transfusion was noted by FAGET and POGGE (p. 297) in the treatment of leprosy. It was thought that this treatment might prove valuable in the hypoproteinaemia and nephritis of leprosy but the results were disappointing.

SHAMA RAO (p. 393) describes a simplified method of preparing iodized *Hydnocarpus* oil for details the original abstract should be consulted. DEGOTTE (p. 394) could not obtain chaubmoogra oil in the Belgian Congo during the war and experimented with an oil obtained from a common plant containing citronella. The results of treatment with this oil were reasonably satisfactory. ROIG and RODRIGUEZ DE LA CRUZ (p. 214) discuss the oils of the Cuban *Flacour* *ciacore*.

COT LESMES (p. 44) has used diphtheria toxoid in the treatment of leprosy and reports favourably on the results especially in lepromatous cases. This finding is in contrast with much of the more recent work on the same lines and with the opinion of TIAN (p. 45) who thinks that this form of treatment shows little promise. He considers leprosy to be curable by general measures of improvement of health and by the use of chaubmoogra oil in high dosage.

DOS SANTOS NEVES (p. 472) has treated a few patients with vitamin A and a chologue with satisfactory results.

*Penicillin* is apparently useless in the treatment of leprosy (FAGET and POGGE p. 646).

ALLER ATUCHA (p. 902) writes strongly in favour of local applications of sulphathiazole in leprosy the drug either as a 15 per cent. jelly or a 10 per cent. suspension in oil or a 15 per cent. watery emulsion is applied to the skin after it has been scraped, or to ulcers. Lesions of the eye may also be treated with these preparations and treatment with injected sulphathiazole along with injections of chaubmoogra oil is apparently useful for generalized lesions.

In trials of sulphanilamide given by injection in rat leprosy CHORINE and CHABAUD (p. 298) have failed to find evidence of any effective therapeutic action but local application of sulphanilamide in the treatment of ulcers and burns in leprosy and treatment of the ocular lesions (keratitis, irido-cyclitis etc.) with a preparation of sulphanilamide have given encouraging results in the hands of CHORINE (pp. 298, 1013).

AMENDOLA (p. 901) has had satisfactory results in ocular leprosy from extirpation of the lachrymal gland. This is not surprising if the glands themselves are infected, but the author has also seen benefit even when the glands showed no evidence of disease.

SAGHER (p. 740) has used Grenz rays in the disfiguring lesions of leprosy with some success.

AMENDOLA (p. 901) discusses tracheotomy in leprosy pointing out that it is not usually an emergency operation. The low operation is to be preferred but there may form a thick muco-membranous exudate below the cannula which is difficult to remove and which may necessitate a second urgent operation for its removal.

Arguing that the cause of perforating ulcer of the foot in leprosy is occasioned only by the loss of sensation and consequent inattention to any wound, SILVEIRA (p. 473) states that ordinary treatment is effective. KIRKALDY WILLIS (p. 740) has performed arterial sympathectomy to promote healing of an ulcer of the foot in a leprosy patient.

#### *Institutions Control.*

BURGESS (p. 298) estimates that throughout the world no less than 15,000,000 people are affected by leprosy either directly by the disease or because they are

dependants of infected persons. He proposes a world federation of communities of infected persons which should be largely self-supporting through organized employment and in which provision should be made for the families infected or not. [The conception of communities in which these people should not be penalized because of a disease for which they are not responsible is growing. These organized communities would not only offer a solution to the troubles of the infected, they would also help perhaps more than anything else to eradicate the disease but they should be attractive.]

DAVEY (p 1013) reports on the work done in the Owerri Province of Nigeria where in a population of 2 000 000 there are probably 75 000 persons suffering from leprosy. Some 18 500 patients have been brought within the scope of the leprosy work directed from the great leper colony and they are cared for either in the central settlement or in the 27 special villages or at over 40 out-patient clinics. Repeated surveys are made and developing cases are discovered and treated while they are in a stage at which treatment is most likely to succeed. There are 20 leprosy inspectors at work in different parts of the Province and their duties include the examination of contacts of infective persons. Already in six areas and with the cordial cooperation of the people themselves practically all infective patients are isolated and receive treatment. In these areas progressive diminution of the incidence of leprosy may be expected. The work has largely been financed by B.E.L.R.A. but the Nigerian Government has now taken it over with the object of extending its scope.

The work of the Oji River leprosy settlement in Nigeria has progressed in spite of the war and MONEY (p 392) states that in 1943 there were 1 187 in-patients. There is a special compound for children. In the surrounding country there are several out-patient clinics at which treatment is given. In the whole Province there are 20 000-25 000 active cases of which 3 000-5 000 are infective. Many of these are segregated in leprosy villages but many more are isolated in their homes.

In the Belgian Congo compulsory segregation of leprosy patients is not advised, but ZANETTI (p 741) states that numerous agricultural villages are being organized, each to provide for 300-400 cases. These are visited each week by a medical officer. Isolation in these villages is more or less voluntary but some mild pressure is applied.

DEKSHAM (p 392) reports on a settlement recently started in Northern Rhodesia.

COCHRANE (p 291) discusses the whole question of leprosy control especially in relation to the Madras Presidency. He advocates surveys of the different communities, night segregation of infective persons in their homes and villages to lessen the infection of children. Institutions should be provided by all municipalities and special sanatoria for children because they cannot be isolated at home. Child contacts should be examined periodically. The Madras Public Health Act is being modified in this sense. No success can be expected unless a well qualified medical officer is placed in charge of the campaign in each province.

SEN (p 1014) refers to a home for leprosy patients which has been founded in India and which is financed partly by private subscriptions and partly by grants from local authorities. It is the first of its kind to be supported in this way by the people themselves. He remarks that many of the inmates had been driven from their homes by their relatives. The home now contains some 300 patients. If similar undertakings were initiated elsewhere some solution of the problem of begging lepers in India might be found.

AUSTIN (p 736) has written an account of the Central Leper Hospital Makogai Fiji. This is very well equipped for treatment and the patients are also employed in certain industries. In recent years 40 patients per annum

have been discharged with only 10 per cent. of relapses. Isolation is compulsory but the conditions are so favourable for the inmates that compulsion is regarded as successful. An account of the work of this hospital during 1943 is given by the same author (p. 294) this cannot further be summarized. This institution is very progressive.

HOPKINS and FAGET (p. 737) have analysed the cases admitted to the National Leprosarium at Carville between 1928 and 1944. Admissions of patients from Texas have increased, and the disease is still endemic in some of the southern States and Mexico though it is declining in the foci in Massachusetts and Minnesota. There are still many white patients some of whom are soldiers infected during various wars. A family history of leprosy is not uncommon where it can be obtained, but conjugal infection is rare. The authors believe that the Kolmer and Kahn tests may be positive in leprosy in the absence of syphilis. The duration of cases from admission to death varied from 9.3 years (lepromatous) to 14.5 years (neural). 145 of the 723 patients were discharged with arrested disease and only 16 relapsed. Most of the discharged patients had neural or tuberculoid leprosy. Most of the deaths were due to nephritis, tuberculosis or leprosy.

WHARTON (p. 737) describes the leprosy hospital at Mahanua, British Guiana. From this institution a programme of contact examination is being conducted. As a result of examination of children a number of early cases have been detected.

SLOAN (p. 296) claims that the policy of compulsory segregation has been effective in Hawaii and quotes the decline in incidence since 1890 in support of his contention.

### *Rat Leprosy*

FIELDING (p. 903) has made a careful study of rat leprosy. He has demonstrated heavy infections of the stomach, and related these to the heavy excretion of leprosy bacilli in the faeces. Repeated inoculation of the skin with emulsions of rat leprosy bacilli is capable of causing extensive invasion of the skin and the bacilli have been found in those parts of the skin which come into contact with the ground, and therefore potentially with infective material. This creates a link between soil contamination and dissemination of the disease. The results of Fielding's work also indicate that rat leprosy bacilli from faeces, urine and primary ulcers are more virulent than those from granulomata and ulcers of long standing. For the production of superficial lesions there must be repeated inoculation, or injection of the organisms and the use of bacilli of high virulence. In natural conditions infection is doubtless due to repeated contact with soil infected by faeces containing the organisms but may also be carried by rat lice. Hookworm larvae can also introduce the bacilli, but faecal organisms introduced by the mouth failed to infect.

LINARES (p. 1014) discusses possible routes of infection in rat leprosy and shows that he has been able to infect fowls by feeding them on rat leprosy material or by injecting it and pigeons by infection.

DHARMENDRA and MUKHERJI (p. 903) found that sulphapyridine given by the mouth, had no effect on rat leprosy.

Charles Wilcocks

## MALARIA.

BIRRELL N. Y. A Case of Indigenous Malaria in Northern Ireland. *Brit Med J* 1946 Apr 27 649-50

A member of the W R N.S with *P. vivax* malaria was admitted to hospital in Londonderry on July 16th 1945. The author advances sound reasons for his belief that infection had been contracted locally. *A. maculipennis* [variety not named] was found breeding in the locality. There were numerous cases of malaria under treatment among members of the Services and the spring of 1945 had been unusually mild. Norman White

COLLINS R. H. Rural Malaria its Epidemiology and Prevention. A Study of refugees who entered the area. *Turkische Ztschr f Hyg u Exper Biol* Ankara. 1941 v 2 No 2 17-23  
Turkish version 5-16

The author reports an outbreak of malaria in Sincanlı, Turkey in a group of refugees who entered the area. *Anopheles maculipennis typicus* and *A. superpictus* were present. All three types of parasite were found. *P. malariae* being relatively common in the small series recorded. Charles Wilcocks

DUKHANINA N. N. [Carriers of *Plasmodium vivax* in the North under Mass Chemoprophylaxis.] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 5 63-76 1 fig [In Russian.]

Observations were made on the carrier-state in malaria (*P. vivax*) among the population of the Archangel Province in northern U.S.S.R. [61-62° N Lat.] The special objects of the investigation—apart from the general characteristics of the carrier-state in the north—were the conditions under which infected persons become carriers the effect of treatment causes of repeated carriage and density of parasites in carriers as compared with that in persons with clinical symptoms.

In the village (Telegovo) selected for this investigation the highest percentage of carriers among the persons examined was 9 per cent. in 1939 the lowest 0.5 per cent in 1940 while in 1941 there was not a single carrier the decline being correlated with an amelioration of the epidemiological position. Carriers were found both among persons affected with malaria in the preceding and in the current year (12.6 per cent.) and among those who had no malaria but were equally exposed to infection (4.5 per cent.) In 73 per cent of cases carriers were detected in the pre-epidemic period, and only 27 per cent in the epidemic period. Among persons who had undergone drug prophylaxis parasite-carriers made up 42-44 per cent. of the total number of cases of malaria. As a rule the carriers were persons who had received insufficient drug treatment. The number of parasites in the blood of carriers is considerably lower than in acute cases in 90 per cent of cases not exceeding one parasite per field of the microscope. C. A. Hoare

SOUTH AFRICA UNION OF Malaria Areas in the Union of South Africa. A Map of the Malarial Survey by the Department of Public Health of the Union (in collaboration, in the case of Swaziland with the Swaziland Administration) 1938. 1941 Pretoria Govt. Printer

The scale of this map is 15 77 miles to the inch. On it are shown four areas —  
A In which the risk of infection is continuous  
B In which it is serious and in which epidemics occur during summer  
C In which a summer epidemic occurs each year but of milder type  
D In which epidemics occur occasionally

Area A is found only in one district of the east coast near the border of Mozambique. Area B covers the north and east of the Union with Area C to the south and west of Area B. Area D lies again to the south and west of Area C, and reaches Pretoria, Witbank, Newcastle and Durban. The remainder (and greater part) of the Union is apparently not affected by malaria.

It is explained that the areas are only approximately correct. They are shown in 4 colours and are very clearly marked. This is a useful map for the malarologist: it measures some 3 ft. 8 in. by 3 ft. No price is quoted: the map was produced for official purposes.

Charles H. Hocks.

MUSPRATT J. Experimental Infection of the Larvae of *Anopheles gambiae* (Dipt., Culicidae) with a *Coelomomyces* Fungus. [Correspondence.] *Nature* 1946 Aug 10 202

CARTER, H. F. Ceylon Anopheline Mosquitoes and Malaria. *Ceylon Health News*. 1945 July-Sept v 12, No 1 5-8

CHI HO. The Anopheline Fauna of Szechuan Province. *Acta Brevia Sinensis* 1945 No 10 1

McARTHUR J. N. Malaria Transmission in Borneo. *Lancet* 1946 July 27 117-18.

Before 1939 it was assumed that the epidemiology of malaria in Borneo was similar to that in Malaya and that the disease was carried mainly by *Anopheles maculatus*. Epidemiological survey in 1939 to some extent supported this assumption except that one village was inexplicably relatively free from the disease despite the presence of abundant *A. maculatus*. An investigation, to explain this revealed a general scarcity of *A. maculatus* in malarious villages and later work showed that this mosquito fed predominantly on animal blood and was therefore unlikely to be a vector. Further work showed that only one species *A. leucosphyrus* had a preference for human blood. It was recovered in numbers from human-bait traps and on dissection 25 specimens were found to be positive [the number dissected, and the numbers with sporozoites and oocysts are not stated]. 2 700 dissections of other species including *A. maculatus* were negative.

*A. leucosphyrus* appears to be the most widely distributed mosquito in Borneo. It enters houses after midnight, feeds on the sleeping inhabitants and leaves before dawn so that it is rare in daytime catches. It breeds entirely in the jungle and is easily controlled by localized jungle clearing around its breeding places and thus is probably the simplest method of preventing malaria in Borneo. In contrast to Malaya where the land becomes malarious after the clearing of jungle and the consequent introduction of *A. maculatus*.

The author concludes that though *A. leucosphyrus* is often said to be harmless yet wherever it has been studied in adequate numbers it has always been found positive on dissection and that it may prove to have much more relation to malaria in other parts of the world than has hitherto been supposed, its presence being masked by its elusiveness and its virulence by the presence of some other much more easily captured and incriminated mosquito.

G. Macdonald.

Downs W G & PITTENDRIGH C. S. Bromeliad Malaria in Trinidad, British West Indies. *Amer J Trop Med* 1948 Jan v 28 No 1 47-68 7 figs [20 refs]

This is an admirably concise and complete account of the complicated problems attendant upon the control of malaria transmitted by bromeliad breeding anophelines of the subgenus *Kerteszia* in Trinidad. The history of investigations on bromeliad malaria is outlined. In 1935 DE VERTEUIL [this *Bulletin* Supplement 1938 v 33 281] published a detailed malaria survey of cacao-growing areas of Trinidad and concluded that the high malaria incidence and mortality of these areas was due to *A. bellator*. This conclusion was subsequently fully confirmed by ROZEBOOM and LAIRD [this *Bulletin* 1942 v 39 664] and by DOWNS GILLETTE and SHANNON [this *Bulletin* 1944 v 41 445].

Throughout a large part of the centre of Trinidad forest has been replaced by plantations of *Theobroma cacao* (cocoa). The cacao trees are protected by tall regularly interplanted shade trees immortelles *Erythrina glauca* and *E. micropteryx*. The plantations as a whole constitute an extensive artificial forest which supports a large human population. The immortal trees are very heavily parasitized by bromeliads. Thirty four species of bromeliads have been found on these shade trees of Trinidad cacao estates five of these species are universal being found on almost every tree. On 50 sample trees the average number of bromeliads per tree was 60. The number of immortal trees to the acre varies from 11 (in abandoned areas) to 64. The different bromeliads are by no means of equal value as host plants of *A. bellator* there is a host plant selection on the part of this anopheline. The two commonest large bromeliads are *Aechmea nudicaulis* and *Gravisia aquilega* they form nearly a half of the total immortal community of bromeliads. *Gravisia aquilega* is by far the most important it is rare to find a plant that does not contain *A. bellator* larvae. It is equally rare to find *A. bellator* larvae in *Aechmea nudicaulis*. *A. bellator* does not occur in all the parts of Trinidad where cacao estates exist but is restricted to areas of high rainfall.

*A. bellator* occasionally enters dwellings to feed, but it leaves for forest cover immediately after feeding. This behaviour precludes the possibility of control by spray killing adult mosquitoes. It has a well-marked evening flight but is active throughout the day in cacao plantations. The greater part of malaria transmission takes place either in the plantations where labourers are freely attacked especially on damp days or on the verandahs of houses in the evening.

As a malaria control measure the manual removal of bromeliads has been tried, but it is excessively costly. Moreover immortal trees are difficult and dangerous to climb. Large thorns cause bad scratches or open lacerations. scorpions spiders and snakes are harboured by the epiphytes. the limbs of the tree are extremely brittle and climbing is almost impossible when the tree is wet.

Spraying with copper sulphate solution can destroy bromeliads. a heavy spraying equipment developed by the U.S. Department of Agriculture for the control of the gypsy moth has been used with success.

A change in agricultural practice whereby shade trees are abandoned and the cacao trees protected by rows of trees planted perpendicular to the prevailing wind, is now being encouraged by the Government of Trinidad. For such windbreaks the mango tree would be suitable. Should this change materialize endemic bromeliad malaria should disappear from the centre of the Island.

Norman White



4. Blood protein tyrosine was elevated in many cases of acute epidemic hepatitis."

MOST H. & HAYMAN J M Jr. Uncommon Clinical Manifestations of Vivax Malaria. *J Amer Med Ass.* 1946 Feb. 23 v 130 No. 8 480-85

Delayed primary attacks of malaria in the returned serviceman some time after the cessation of effective suppressive treatment may be bereft of the symptoms which characterize a typical attack and it may not be possible to find parasites in blood smears for some days. Persistence and patience in the examination of blood smears may result in finding *P. vivax* and useless treatment with penicillin or sulphonamides may thus be avoided.

Symptoms and signs suggestive of an abdominal disease may precede or accompany an acute attack of vivax malaria. blood smears should be examined carefully before recourse is had to surgery. The white blood cell count is rarely increased in malaria.

Convulsions may occur with attacks of vivax malaria as a reaction to hyperpyrexia or in patients with underlying brain disease. Pre-existing epilepsy head injury and *falciparum* malaria must be excluded. A stiff neck and fever may simulate meningitis.

Urticaria or severe angioneurotic oedema may precede or accompany acute attacks of vivax malaria.

Pulmonary signs and symptoms in attacks of vivax malaria may suggest a diagnosis of pneumonia in the winter months.

Surgical operations or trauma may reactivate vivax infections long after the last clinical manifestation of malaria.

Malaria does not exclude the possibility of other co-existing infections.

Norman White

Downs W G. Results in an Infantry Regiment of Several Plans of Treatment for Vivax Malaria. *Amer J Trop Med* 1946 Jan. v 26 No 1 67-86  
4 figs

This report deals with the experience of two battalions of an infantry regiment which were for periods of 189 and 164 days in 1942-43 on Guadalcanal a highly malarious island, and thence were transferred to Samoa which is malaria free for demalarialization. While in Guadalcanal, first quinine and then mepracrine suppressive therapy was administered but was not rigidly enforced except in the last two months of the regiment's service on that island. Forty-eight per cent. of the regiment suffered from malaria in Guadalcanal, and the monthly malaria incidence rates varied from 800 to 1,500 per 1 000 per annum. most of the diagnoses were clinical.

For demalarialization in Samoa where there were laboratory facilities different groups of men were subjected to different treatments. The results are recorded in detail. The conclusions are summarized as follows —

In troops almost universally infected with vivax malaria few or no individuals were cured of infection by suppressive atabrine therapy (0.4 gm. per week) administered for a period of six months during exposure on a malarious island.

Few or no cases of vivax malaria were cured by mass therapy with atabrine or with atabrine plus plasmodochin after leaving the malarious island.

"Initial attacks of malaria occurred as late as six months or more after discontinuing atabrine suppression or after mass therapy of any of the types employed.

"Atabrine mass therapy did not alter appreciably the number of first relapses occurring after first observed attacks.

There was a definite tendency to relapse between the fifth and seventh week after the first observed attack with a sharp peak in the sixth week. No difference in course of disease was noted between the group which had had malaria attacks previously on the malarious island and had first observed attacks during the course of this study and the group which had not had malaria attacks on the malarious island and had actual primary attacks during the course of study. (The total time span from date of first exposure to infection to termination of study was one year)

Plasmochin administered as a part of mass therapy apparently aided in lowering the peak rate of first observed attacks and spread the experience over a longer time period without appreciably altering the final outcome as far as first observed attacks and first relapses are concerned. There may have been a slight tendency to lower the ratio of total relapses to first observed attacks but this point is far from being clearly established and needs observation over a longer period of time

HAO W E The Quinine-Oxidizing Enzyme and Liver Aldehyde Oxidase  
J Biol Chem 1946 June v 163 No 3 699-711 4 figs [16 refs.] Norman White

A derivative of quinine was obtained by KELSEY *et al* [this Bulletin 1944 v 41 923] when minced rabbit liver was incubated with the alkaloid. It was shown by MEAD and KOEPLI [this Bulletin 1945 v 42 9] to be an oxidation product of the parent substance in which the hydrogen atom in the position adjacent to the nitrogen atom of the quinoline nucleus had been replaced by a hydroxyl group. The enzyme involved has now been prepared in approximately 5 per cent purity and its activity determined under standard conditions by the rate of reduction of methylene blue in the presence of cinchonidine as substrate. Rabbit liver was found to be the only satisfactory source of the enzyme which has been shown to oxidize quinoline isoquinoline and pyridine rings in the corresponding position to that found for quinine. The rate of oxidation was dependent on the reactivity of the hydrogen atom in that position. It is possible that the slower oxidation of certain substituted quinolines by enzyme action may help to explain their antimalarial activity. Plasmogunone and substances with other heterocyclic or aromatic rings were not oxidized by this enzyme which has properties similar to those of liver aldehyde oxidase. It is soluble in water resistant to a temperature of 60°C for five minutes and is precipitated at 25-40 per cent saturation with ammonium sulphate. In properties it resembles a similar preparation from pig liver. Whereas that from rabbit liver could oxidize quinolines as well as aldehydes the other preparation reacted with aldehydes only. The enzymes from the respective sources are both flavo-proteins. No separation of the substances involved in the oxidation of quinolines or aldehydes could be achieved, and in the presence of both types of substrate the rate of reaction was slower than with either type alone. The mutual interference by the two substrates suggests that both reactions share a common element in the pathway of oxidation which available evidence suggests to be the flavin group

J D Fulton

MOST H & HAYMAN J M Jr Relative Efficiency of Quinacrine (Atabrine) and Quinine in Treatment of Acute Attacks of Vivax Malaria. Amer J Med Sci 1946 Mar v 211 No 3 320-24 2 charts

Three hundred and ninety-seven patients with acute attacks of *P. vivax* malaria with fever and parasitaemia were treated with mepacrine (quinacrine). All treatment was begun on the day following the onset of the attack. On the first day of treatment 1 gm of mepacrine was given by mouth, in three divided

doses. On the succeeding six days 0.1 gm. was given three times a day after meals. The total dose given over the seven-day period was thus 2.8 gm. Parasite counts were done twice daily and continued till negative for three consecutive days. Plasma-mepacrine levels were determined on the 2nd and 8th days. The patients left the ward on the 8th day and 200 of them were observed for 120 days or till relapse. During this time smears were examined twice weekly. A rise of mouth temperature over 100°F associated with parasitaemia was considered a relapse and the patient was re-admitted to hospital.

One hundred similar patients were treated with quinine the treatment starting the day after the onset of the attack. On the first day 1 gm. was given thrice at intervals of 8 hours. On each of the following 13 days 2 gm. were given in three divided doses. Thus 29 gm. of quinine sulphate were given by mouth during the 14 days. Minimum and maximum plasma-quinine determinations were made on the 2nd, 7th and 14th days of treatment. The other observations were the same as described for the mepacrine group.

Mepacrine cleared the peripheral blood of parasites more rapidly than did quinine. At 48 hours from the commencement of treatment, 77 per cent. of the mepacrine patients were free from parasites as compared with 44 per cent. of the quinine patients.

Of the patients treated with mepacrine 7 per cent. had fever of 100.2 or higher on the 2nd or 3rd day of treatment, as compared with 10 per cent. of those treated with quinine. In the treatment of delayed primary attacks of *river malaria*, 32 per cent. of patients treated with quinine had fever on the 2nd or 3rd days as compared with 16 per cent. of similar patients treated with mepacrine.

All concerned with these observations were agreed that mepacrine is more effective than quinine in the prompt control of symptoms of an acute attack of *malaria*.

With regard to toxicity the only points in favour of either drug are the absence of tinnitus with mepacrine. Rare cases of idiosyncrasy or sensitization to either drug may occur. Patients with eczematoid or exfoliative dermatitis and acute *malaria* should not be given mepacrine if they have had the drug before.

Eighty per cent. of Pacific infections relapsed within the 120 days of observation regardless of the drug used in treatment. The mean interval to relapse after mepacrine was 63 days, and after quinine 22 days.

The observations show that mepacrine is superior to quinine in the treatment of acute attacks of *river malaria*.

Norman White

TOOMEY A. G. Aspects of the Treatment of Subtertian Malaria. *J. Roy. Nav. Med. Serv.* 1946 Jan v 32, No 1 32-8 1 fig

This paper is based on the treatment of 883 adult European patients suffering from *P. falciparum malaria* in Freetown, Sierra Leone during 1943-44. Various forms of treatment are compared. Mepacrine was preferred to quinine, relapses were fewer after its use. The average amount of mepacrine given in a twelve-day course was 5.4 gm. 1.2 gm. the first day, 0.9 gm. the second day, 0.6 gm. the third day, and 0.3 gm. daily thereafter till the end of the course. In 157 cases the dose of mepacrine was doubled on each of the last four days of the course during which the patient was given graduated walking and running exercise. When necessary mepacrine was given by both intramuscular and intravenous routes without any ill effect. It was preferred to quinine similarly administered. After the introduction of mepacrine as a suppressive, pamaquin was badly tolerated and its use in treatment was discontinued. [Pamaquin is

said to have been given in doses of 0.1 gm. thrice daily for four days probably a misprint for 0.01 gm.]

Norman White

GORDON H. H. MARBLE A. ÉNGSTROM W. W. BRUNSTING H. A. & LIPPINCOTT S. W. Relapses following Delayed Treatment of naturally Induced Vivax Malaria of Pacific Origin. *Science* 1946 Mar 29 391-2. [10 refs.]

Sixty nine white soldiers who required malaria therapy for neurosyphilis were infected with U.S. anophelines which had previously been fed on soldiers infected with *P. vivax* malaria acquired in the Pacific area. Antimalarial treatment (2.8 gm. mepacrine in 6 days) was delayed in the patients suffering from neurosyphilis until they had had from 8 to 15 paroxysms with an average of 40 hours of fever over 104° F. This level was reached on the average in 20 days during which blood smears revealed *P. vivax*. The patients were then observed till a relapse occurred or for at least 60 days without a relapse. Thick blood smears were examined twice weekly.

Forty five patients (65 per cent.) had a relapse. There was no significant difference between the mean hours of fever above 104° or between the mean days of parasitaemia in those patients who relapsed and those who did not. The relapse rate was not markedly different in another group of 124 patients suffering from Pacific *P. vivax* malaria whose attacks were promptly treated with mepacrine in the Harmon General Hospital.

Seventy-six per cent. of the relapses following delayed treatment occurred within 59 days and 93 per cent. within 89 days of the termination of treatment.

Relapses occurred in men infected with 7 of the 10 strains of *P. vivax* used. Only 7 men had been infected with the 3 strains that caused no relapse. The importance of the strain in determining relapse rates is illustrated by the fact that only 2 of 16 soldiers infected with *P. vivax* of the Mediterranean origin relapsed and these after intervals of 111 and 189 days from the termination of mepacrine treatment. No relapse followed the primary manifestations of infection induced in 28 men by the intravenous inoculation of trophozoites of Pacific strains which had caused very high relapse rates when infection had been conveyed by mosquito bite. No evidence was forthcoming that early treatment of malaria attacks delays the development of immunity.

Norman White

GINSBERG J. E. & SHALLENBERGER P. L. Wood's Light Fluorescence Phenomenon in Quinacrine Medication. *J Amer Med Ass* 1946 July 8 v 131 No 10 808-9

Ginsberg accidentally observed that his finger nails emitted a bright greenish-yellow fluorescence when he was examining a child for tinea capitis under Wood's light. He had recently returned from the tropics and presumably his skin and its appendages were still stained with mepacrine. Shallenberger had made a similar observation whilst making an earlier study concerning deposits of the drug in the hard palate and finger nails (*Arch Dermat & Syph* 1946 v 53 349).

These authors collaborated in a study of 511 patients. 158 of whom had taken mepacrine. In 79 of the latter the greenish yellow fluorescence did not occur but 55 had not taken the drug for 13 months. On investigation it was found that the characteristic fluorescence occurred in all subjects who were on mepacrine therapy or "sound prophylaxis". The fluorescence could be noted for three to six months after the drug was discontinued, but as the nails grew the proximal areas showed the normal fluorescence of healthy nails (violet blue in colour) whilst the distal parts showed the greenish yellow hue referred to above.

The toe-nails cleared more slowly than the finger nails frequently the nails of the big toes remained fluorescent longer than the others sometimes for as long as a year after mepacrine therapy or prophylaxis ceased.

Unusual fluorescence phenomena did not occur in patients receiving numerous other drugs including penicillin and sulphonamides.

Mepacrine tablets and aqueous solutions have a brilliant yellow fluorescence under Wood's light.

The authors suggest that there is a longer delay in the complete excretion of mepacrine from the body than has previously been reported, and consider that their observation confirms that made by LUTTERLOH and SHALLENBERGER (references quoted above) concerning mepacrine deposits which may be seen as bluish pigmentation under the nails when examined in daylight.

[Wood's light—so called—is an ultra violet ray filtered through glass containing nickel oxide (Wood's glass) which restricts the passage of all but relatively long wave ultra violet light of about 3 650 Å the light is commonly used for the rapid diagnosis of tinea capitis since hairs infected with *Microspora* emit a characteristic green fluorescence

R. M. B. MacKENNA

KIERLAND R. R. SHEARD C. MASON H. L. & LOBITZ W. C. Fluorescence of Nails from Quinaertine Hydrochloride. *J Amer Med Ass* 1946 July 6 v 131 No 10 809-10 1 fig

Kierland who had just returned from the south-west Pacific area where he had been taking mepacrine daily for almost two years, noted a brilliant yellow-green fluorescence of his finger nails under Wood's light. He and his colleagues have noted this phenomenon in nine other persons all of whom had taken mepacrine for from 5 to 21 months. They noted that the fluorescence begins to fade three months after the drug is discontinued, and that it usually disappears in six or seven months. In their opinion the blue-black pigmented areas of the nailbeds and hard palate which have been noted in persons taking mepacrine for long periods do not fluoresce neither does the skin or hair of these subjects further their teeth do not show an abnormal fluorescence.

The exciting wavelength of the Wood's light used in this study was 3 500-4 000 Å the wavelength of the light emitted by the fluorescing nails was 5 400-6 000 Å. The fluorescent wavelength of solutions extracted from the skin nails and hair of a person receiving mepacrine was 5,300-5,800 Å. Quantitative photofluorometric determinations were made of the skin and its appendages in three persons. The results are tabulated thus —

*Mepacrine in Micrograms per Gram of Tissue*

Nails		Hair		Skin	
1	2.6	1	27.2	1	10.4 wet weight
2	5.2	2	47.6		28.1 dry weight
3	0.63				

This person had discontinued taking mepacrine three and a half months before the clippings of nail were obtained.

The authors suggest that it would be interesting and valuable to determine the amounts of mepacrine in the affected and non-affected areas of skin of persons with the atypical lichen planus syndrome.

R. M. B. MacKENNA.

LIPPINCOTT S W ELLERBROOK L D HESSELBROCK W B CARRICO C C & MARBLE A The Relationship of Spinal Fluid to Plasma Concentrations of Quinacrine and Quinine *J National Malaria Soc* Tallahassee Fla 1946 Mar v 5 No 1 85-91

The concentration of quinacrine (atebrin mepacrine) and quinine has been simultaneously determined in the plasma and spinal fluid of two groups of neurosyphilitic patients as a guide to the mode of action and effectiveness of these drugs in cerebral malaria. In one experiment 51 patients divided into 7 groups were given quinacrine in the form of atebrin dihydrochloride in doses ranging from 0.5 to 3.0 gm. over a period of 1-3 days so that the plasma concentrations equalled or were greater than those obtained during therapy. These concentrations were maintained for different periods the range encountered being from 18 to 135 micrograms per litre for plasma and from 0 to 6 micrograms per litre in the case of spinal fluid, the values for a large percentage of the latter being within the range of error of the method. Specimens of plasma and spinal fluid were obtained from 2 to 61 hours after the last dose of drug the latter being withdrawn immediately prior to the venous blood specimen. The method of BRIDIE and UDENFRIEND [this *Bulletin* 1944 v 41 453] was used for the estimation of atebrin after trial and with slight modifications for quinine. In spinal fluid, the concentration of quinacrine varied from 0 to 15 per cent of that in plasma and the ratio was not appreciably affected, in the different groups by variation in conditions of dosage and withdrawal. In similar experiments quinine sulphate dihydrate was given to 44 subjects in doses ranging from 0.5 to 3.0 gm. during twenty four hours. Specimens were obtained from 2.0 to 3.5 hours after the last dose. The plasma levels at their peak values varied from approximately 1 000 to 7 000 micrograms per litre in six different groups on different dosage schedules. The corresponding variations in spinal fluid level were from 19 to 260 micrograms per litre. The maximal ratio of the latter to that in plasma in one case reached 9 per cent but was generally much lower. It appears that the ratio increased in proportion as the plasma concentration was increased, and as the time of maintenance of the latter lengthened. The authors believe that the mechanism of exchange of quinacrine between plasma and spinal fluid is one of diffusion. Both drugs are probably bound to protein in plasma and hence the smallness of the spinal-fluid/plasma ratio. It is doubtful if the concentrations of quinacrine and quinine in the spinal fluid obtained with the non toxic doses used could be of therapeutic value in cerebral malaria if these drugs were in combination with protein. *J D Fulton*

WILLIAMSON ANNE HEGSTED D M McKIBBIN J M & STARE F J The Effect of Variations in the Level of Dietary Calcium upon the Growth of Young Rats receiving Atabrine *J Nutrition* 1946 June 10 v 31 No 6 647-55

When recently weaned male rats were given a standard diet to 100 gm of which 40 to 60 mgm. of mepacrine was added the rate of growth was significantly lowered as compared with that of controls given no mepacrine. This inhibition of growth was more marked when the diet contained 1.35 per cent. of calcium than when it contained either 0.55 or 0.15 per cent. The concentration of mepacrine in the liver was much greater in animals given the high calcium diet than in those given the low calcium diet although the intake of mepacrine was approximately the same in the two groups. The concentration of mepacrine in the liver was the same after 30 days and after 63 days of treatment.

The reaction of the contents of the distal small intestine and caecum was more alkaline in the animals taking the high calcium diet. The addition of various

salts to the diet failed to show any effect of alteration of intestinal pH upon the toxicity of mepacrine. Some animals on the high calcium diet exhibited renal calculi which may have impaired the excretion of mepacrine. It is therefore not clear whether the increased toxicity of mepacrine when combined with a high calcium diet is due to increased absorption, decreased excretion, or to a specific effect of calcium on mepacrine metabolism. *H E Harding*

IMPERIAL CHEMICAL (PHARMACEUTICALS) LIMITED. BIOLOGICAL DEPARTMENT  
Paludrine—a Summary of Information to February 1946 [DAVEY D G]  
1946 Mar 1 13 mimeographed pp. [19 refs.] [Report No BT 1166.]

This is a most useful summary of information about Paludrine. Work on this drug is still being continued because there are points on which insufficient information exists but this account by bringing together all the available results of investigation, presents a picture which will be of very great value to those who work on the chemotherapy of malaria and no less to those who must plan ahead for treatment policies.

To attempt an abstract of this already condensed summary would scarcely be possible—it is enough to indicate briefly some of the conclusions which existing work permits. The author assumes by analogy that exo-erythrocytic forms of the human malaria parasites exist, though he admits that they have not yet been found.

Two salts of Paludrine have been used the monohydrochloride and the monoacetate each is sparingly soluble in water. The fatal dose for acute poisoning in animals is from 25 to 60 mgm. per kgm. for chronic poisoning from 20 to 60. Paludrine is rapidly absorbed and excreted, chiefly in the urine though the blood concentration is much diminished 12 hours after administration, a build up may be effected if doses are taken twice each day.

In man one to three daily doses of 100 mgm. or less [these are total doses, not doses per kgm.] may completely and permanently prevent *P. falciparum* from gaining access to the blood stream even if taken on the day after exposure to infected mosquitoes. There is evidence of an inhibitory action on the presumed exo-erythrocytic forms of *P. vivax* but the fact that relapses do occur after cessation of this treatment shows that the action is not lethal.

The suppressive effect of Paludrine is almost perfect—a daily dose of 25 mgm. is enough completely to suppress subtertian, and of 100 mgm. to suppress benign tertian, malaria. Moreover since a single dose of 100 mgm. is enough to control a clinical attack so that relapse does not occur for several weeks the same dose given once each week, is likely to be an efficient suppressive dose.

In man, slight toxic symptoms may be produced with 500 mgm. twice daily for 28 days—single doses of more than 750 mgm. should not be given. In treatment it is wise to distinguish between clinical cure and radical cure. In subtertian malaria the former can be achieved by a single dose of 100 mgm. or by repeated doses of 50 mgm. the latter by 100 mgm. t.i.d. for 10 days. In benign tertian malaria clinical cure can be achieved by similar doses but radical cure cannot be guaranteed—relapses do occur though with bigger doses up to 500 mgm. twice daily for 14 days patients are apparently slow to relapse. After treatment patients may be released with a supply of Paludrine to be taken as a weekly dose of 100 mgm. for several months. In quartan malaria Paludrine apparently has good effect but there have been too few cases to make general claims. Intravenous injections have been used, and in subtertian malaria a dose of only 5 mgm. given by this route has marked effect.

Paludrine does not destroy gametocytes but renders them non-effective for mosquitoes for several days—this seems to be due to the action of the drug while in the stomach of the mosquito.

The author quotes much already published work, most of which has already been abstracted in this *Bulletin* Charles Wilcocks

MOST H LONDON I M KANE C A LAVIETES P H SCHROEDER, E. F & HAYMAN J M Jr Chloroquine for Treatment of Acute Attacks of Vivax Malaria. *J Amer Med Ass* 1946 July 20 v 131 No 12 963-7 5 charts

A report on the activity of the antimalarial drug chloroquine (SN 7618) 7-chloro-4-(4-diethylamino-1 methylbutylamino) quinoline which was recently synthesized in America has been reviewed [this *Bulletin* 1946 v 43 708] In the present study its value in the treatment of acute attacks of malaria due to infection with *P. vivax* acquired in the Pacific and Mediterranean theatres of war has been investigated in primary and relapse cases. More than 500 patients were treated whom it was possible to follow up until relapse occurred or for a period of 120 days after the end of treatment. The cases were grouped according to origin and stage of infection. Several dosage schedules were employed in which 0.8-2.0 gm of the drug was administered and 50-75 cases were treated in each group. The schedules in which 1.0 gm was given on one day 1.5 gm. in 4 days or 2.0 gm. in 7 days proved satisfactory. Comparison was also made of the results obtained in patients treated with 2.8 gm. quinacrine (atebrin) during a period of 7 days or with 29.0 gm. quinine during 14 days. It was found that chloroquine freed the peripheral blood from parasites abolished fever and controlled other symptoms more rapidly than the other two drugs. No major toxic manifestations were caused by chloroquine but about 20 per cent. of the patients had general or localized pruritus of a slight or transient character. In 2 per cent. pruritus was accompanied by skin eruptions. Relapse rates 120 days after treatment were slightly lower than with quinine or atebrin, but these relapses with the new drug occurred much later in the observation period. Malaria acquired in the Pacific was more prone to cause relapses than that acquired in the Mediterranean area and no radical cures were obtained with any of the drugs. Plasma levels of chloroquine are recorded for 176 patients treated as above and it was found that a minimum concentration of approximately 10 micrograms per litre was necessary to control an acute attack. [After therapeutic doses of Paludrine 10-100 micrograms of the drug are present per litre of plasma.] The authors summarize the reasons for their conclusions that chloroquine is a safe and highly effective drug which is superior to quinine and quinacrine under the above conditions of test. A course of treatment for acute attacks of malaria due to *P. vivax* is outlined.

J D Fulton

BARBER, H. J & WRAGG W R. Contributions to the Chemistry of Synthetic Antimalarials. Part II Tetrahydropamaquin *J Chem Soc* 1946 July 610-13

BARBER H. J MAJOR F W & WRAGG W R. Contributions to the Chemistry of Synthetic Antimalarials. Part III. An Open Ring Analogue of Tetrahydropamaquin *J Chem Soc* 1946 July 613-16.

MADINAVEITIA J The Antagonism of some Antimalarial Drugs by Riboflavin. *Biochem J* 1946 v 40 No 3 373-5 1 fig

In an investigation relating to the mode of action of antimalarial drugs the antagonism by these and other compounds of riboflavin an essential metabolite



for *Lactobacillus casei* has been studied. For this metabolite which the organism cannot synthesize and which plays a part in enzyme systems an extraneous supply is necessary. The present indirect approach to the problem was made because of the lack of knowledge of the essential requirements of malaria parasites. The explanation of the action of a drug in some cases appears to depend on the fact that it bears a similarity in molecular shape to the metabolite. Such similarity in structure between riboflavin and certain antimalarials has been indicated by CURD *et al* in this Bulletin 1946 v. 43 394. A suitable medium for the lactobacillus is described, in which growth was measured turbidimetrically. To observe the effect of riboflavin on the inhibition of growth by drugs the former was made up in various concentrations in the medium which was then sterilized and inoculated with the test organism in bulk. To series of tubes containing the drugs for assay in various dilutions was added the medium with the organism and the different concentrations of riboflavin. After incubation the presence or absence of growth was determined. Of the various substances tested, it was found that only those having antimalarial properties were antagonized by riboflavin the effect being most marked at relatively high concentrations of the latter.

J. D. Fulton

- i. TOKKIN Isabel M. & WORK T. S. A New Antimalarial Drug [Correspondence] *Nature* 1945 Nov 24 630
- ii. MUKERJI B. Antimalarial Drugs of the Indigenous Materia Medica of China and India. [Correspondence] *Ibid* 1946 Aug 3 170.

i. The authors have made animal experiments with samples of two Chinese plants reputed to possess antimalarial properties. These were *Fraxinus malacophylla* and a root known as *chang shan* which is reputed to be *Duckroa febrifuga*.

The first plant was found to be without action on *Plasmodium gallinaceum* in chicks. Extracts of the second plant showed considerable activity against a trophozoite-induced infection of *P. gallinaceum* in chicks. No alkaloid could be found in either plant.

ii. Mukerji also tested *F. malacophylla* on simian and human malaria. His observations confirmed those of TOKKIN and WORK (see above) in the case of chicks [although in fact he claims that these authors' observations differed from his since they recorded considerable activity against *P. gallinaceum* in chicks. In fact this statement as will be seen above referred, not to the use of *F. malacophylla* but to *D. febrifuga* (*chang shan*)].

In benign and malignant human malaria Mukerji could find no proved antimalarial effect on the part of *F. malacophylla* using it in three forms but in two of four cases a temporary febrifugal effect with a brief disappearance of the malarial parasites was recorded both cases relapsed.

The same phenomenon was observed with two indigenous Indian drugs *Cassia alata* and *Cassia bonducella*. The author also examined *F. malacophylla* with success in China, and India, and found that indigenous vegetable drugs of slight febrifugal effect were of little value in the treatment of malaria.

O. D. Burke-Gaffney

- i. HEIDELBERGER M COATES W A & MAYER M M Studies in Human Malaria. II Attempts to Influence Relapsing Vivax Malaria by Treatment of Patients with Vaccine (*Pl vivax*) *J Immunology* 1946 May v 53 No 1 101-7
- ii. — PROUT C HINDLE J A & ROSE A S Studies in Human Malaria. III. An Attempt at Vaccination of Paretics against Blood-borne Infection with *Pl vivax* *Ibid* 109-12.
- iii. — MAYER M ALVING A S CRAIGE B Jr JONES R. Jr PULLMAN T N & WHORTON M Studies in Human Malaria. IV An Attempt at Vaccination of Volunteers against Mosquito-borne Infection with *Pl vivax* *Ibid* 113-18 1 fig

1. The authors have attempted to influence the relapse rate in chronic cases of benign tertian malaria by the use of a vaccine prepared from infected blood, as described in Part I of this series [this *Bulletin* 1946 v 43 816]. Three groups of approximately 60 men who had contracted *vivax* malaria in the S W Pacific were used. One group which served as control received only routine treatment with drugs. A second group received drug treatment for the primary attack only and was then vaccinated as described below. The third group was treated like the second, the vaccine in this case consisting of red cell stromata obtained from normal blood by treatment similar to that used in preparing the vaccine from parasitized blood. Some members of the groups had at various times previous to the start of experiment received atabain in suppressive doses. Each group was sub-divided into two according to blood groups as previous experiments of other authors had shown that high  $\alpha$ -agglutinin titres may be immunologically significant in malaria. In the present experiments however no increase of  $\alpha$ -agglutinin was noted in subjects of blood group O after injection of normal or infected blood from group A subjects. The average period of observation of these cases was 7-8 months. The amount of vaccine for each person corresponded to 2-6 billion parasites or an equivalent amount of normal red cell substance. It was given in divided doses by the intracutaneous (10 per cent) subcutaneous (40 per cent.) and intravenous routes (50 per cent.) over a period of 4-5 days. In a few cases 2 or 3 courses of vaccine treatment were given only Rh-negative vaccines and stromata being used on Rh-negative individuals. There were only minor untoward reactions as the result of treatment. It was found that immunization with vaccine or stromata had no effect on the relapse rate.

ii. Previous attempts at active immunization in human malaria with inconclusive results were reported by KONSTANOFF [this *Bulletin* 1930 v 27 663] and by SCHILLING [*ibid* 1940 v 37 368]. The present authors have made the first controlled vaccination experiments against a primary attack of benign tertian malaria. Vaccines were prepared as already described with the McCoy strain of *P vivax*. Three neurosyphilitic white males without previous history of malaria were used in the tests. The vaccine containing a total of approximately 4 billion formalized parasites was administered by the same three routes as in Part II above in two courses lasting 3-5 days with a week interval between each course. The patients were injected with  $\frac{1}{2}$ -5 million parasites of the same strain 19-22 days after the last dose of vaccine. The subsequent results of inoculation were the same in those vaccinated as in controls. Two of the vaccinated were given quinine when the malarial attack developed and further tested for immunity by reinoculation with infected blood 13-16 days later. It was concluded that no protection had been afforded by vaccination.

iii. In this series of experiments protection was attempted against the bites of mosquitoes infected with *P vivax* Chesson strain by vaccines prepared

FOURCHE & RICKLIN [this *Bulletin* 1929 v 26 183] and FOURCHE & HAVZAUX [this *Bulletin* 1932 v 29 305]. Further details are given in the present report. The duration of protection was judged to be about 6 months.

*Results Sector by Sector*—Separate detailed accounts, covering 10 pages of text, are given of the work done in each of nine geographical sectors. These do not lend themselves to summary. References are made to population-displacements found to be necessary in several zones of the Tshikapa-Lutshiko sectors.

In an interesting concluding section the author outlines the way in which mass movements of populations due to dynastic quarrels, inter-tribal warfare, railway and industrial developments, etc., have conduced to the spread of sleeping sickness. Apparently the infection has converged upon Tshikapa, through these population-movements both from the west and from the East.

From the west came the Bampende from the River Kwango installing themselves in the lands of the long-settled lesser tribes and other important invaders were the Lunda. Not long before the arrival of the Europeans a further wave swept over from the west—the warlike Batshok, "*les prussiens de l'Empire*"—kinsmen and rivals of the Lunda, burst into the Kasai, enslaving the populace except for the Bampende who recoiled before the invasion, and it is this movement of the Batshok, in particular to which the author ascribes the spread of infection from the Kwango into the Kasai which was recognized in 1923.

Well over to the east on the banks of the Boshumai and the Lomami, and beyond, the first Europeans put an end to the internecine warfare of the Baluba but ineradicable hatreds and rivalries remained. In order to ensure the authority of the Chiefs recognized by the State it became necessary to separate the dissident groups. They were moved westward, first to Luluabourg, then to Luebo Tshukapa, etc. This was the first wave of infected Baluba tribesmen towards the Kasai. The subsequent building of a railway in the Dibaya and Luluabourg territories gave rise to further population-shifts with still further spread of sleeping sickness into these particular areas from which infection was brought into Tshikapa by the recruitment of labourers.

[There are no detailed references to tsetse flies or to tsetse fly control, in this report.]

E M LOUIS

McLEITCH, J. L. The Control of Sleeping Sickness in Northern Nigeria. *Farm and Forest*. Ibadan Nigeria. 1945 Apr-June, v 6 No 2 69-79

The Anchar Settlement in the Zaria and Kano Provinces of Northern Nigeria has previously been mentioned in this *Bulletin* but the account given by the present author is the first seen by the reviewer in which the administrative details have been fully described. The settlement was conceived as part of the scheme for the control of trypanosomiasis, in view of the fact that control by mass treatment, although highly successful, could not be regarded as a final answer to the problem, in that it seemed impossible by that method alone completely to eradicate the human disease; moreover mass treatment was not applied to cattle. The area of the Settlement was chosen because it seemed probable that complete eradication of tsetse could be achieved and maintained by an effort not beyond the capacity of the population—the corridor which will eventually be rendered free from fly is about 70 miles in length and comprises 700 square miles. In this corridor the people from surrounding (and infested) districts are, or will be concentrated—they will be protected from fly but the fact of concentration and removal to strange surroundings must inevitably introduce new problems, medical, veterinary, agricultural and social. All these

problems must be solved many were anticipated and provided for but others could not be foreseen

The work was started in 1937 with a grant from the Colonial Development Fund of £95 000 to be spread over five years and during the same period the Nigerian Government proposed to increase expenditure on the treatment service by £55 000. The tsetse control staff included 14 Europeans—two entomologists one District Officer one well sinking foreman and ten Control Officers. The scheme was controlled by the Sleeping Sickness Service but a committee from all the departments concerned was created to advise on policy. [Dr McLetchie wishes it to be made clear that Dr H M O LESTER was primarily responsible for the conception of the Anchau scheme and that in the early years of development Dr T A M NASH was in local charge at Anchau.]

In 1938 and 1939 the preparatory work was initiated basic investigations were made and staff was trained. In 1940 and 1941 movements of the population were made into the Settlement and clearings were extended. Thereafter because of the war the work was placed on a maintenance basis until later in 1942 there was a gradual resumption of tsetse surveys research clearing well-sinking and general development.

The amount of work done is indicated in the body of this paper but the great difficulties always met in any attempt to change the habits and customs of an intensely conservative people are hinted at rather than stressed. The peasants are Moslems some lived in reasonably prosperous villages but many were on a bare subsistence level and were not good farmers. Guineaworm infection was rife and contact with tsetse very close. It was necessary to assess the fertility of the land to which the people were to be moved a difficult task since no accurate scientific method of assessment for this area was known. Nevertheless a pointer was recognized by an Agricultural Officer which was the presence of certain trees and the density of growth of grass. Certain plots were cleared and four staple crops planted in each growth and yield were correlated with soil and vegetation types and the association of the trees mentioned above with fertile soil was established. New village sites could now be chosen after extensive survey and mapping had been done. Land was divided among the householders according to native practice by the headmen of the hamlets. Compounds were dispersed singly or in groups the layout now advised is a group of houses round a central well-space 100 feet square. The compounds themselves are 100 feet square and are separated from each other by a space of 100–125 feet. Huts are 12 feet in diameter and 12 feet apart.

In the first period the technique of stream clearance was standardized and over 300 miles of stream were cleared. Within the Settlement area streams are partially cleared mahogany and other valuable high branching trees being left at intervals. To prevent re-infestation of these streams by tsetse from the uncleared rivers outside the corridor a barrier clearance straddles the corridor boundary. The barrier is a mile in length 50 to 100 yards broad and is cleared ruthlessly.

The sinking of wells and the protection of well-heads was carried out on a large scale. Fruit trees and other sources of foodstuffs were introduced and the disposal of rubbish and animal manure was given attention.

In the dry seasons of 1940 and 1941 the major population movements were made water supplies were improved and anti tsetse clearances were extended. By the second year 16 new villages and seven extensions to existing villages were completed. Pit latrines were introduced to all compounds and the authorities insisted on their use and care. The value of a combination of partial and barrier clearance was now proved and clearing was therefore extended. The organization of annual re-flashing of already cleared areas was even more

laborious than initial clearing this is done on a communal basis and requires about four days work from each adult male. Villagers re-slash well the more sophisticated people of large towns badly. Moreover people from the shums of old Anchan did not cooperate well, and were poor farmers. Experiments with new crops were made and continued and an estimate of fuel requirements (15 cwt of wood per person each year) was made and fuel areas calculated accordingly were marked out.

Cotton and ground-nut markets were opened, the preparation of hides for export was taught, soya cultivation was introduced and sugar production encouraged. Cattle were inoculated against rinderpest but trypanosomiasis interfered seriously with the cattle programme. This disease was transmitted, not by tsetse but by other blood-sucking flies. Fodder for livestock became scarce but arrangements were made to cultivate it.

By the end of 1942 the people had accepted their new life cheerfully but continued supervision was very necessary. After that the programme of expansion in abeyance for 18 months was resumed and improvements were made within the corridor. A demonstration farm was opened and schools were started in all districts and in many villages.

The only human diseases mentioned in this paper are cerebrospinal meningitis, smallpox, guinea-worm and trypanosomiasis. Outbreaks of the first two occurred but were controlled, and the value of treatment for meningitis and of vaccination for smallpox, are apparent to the people. Guinea-worm which creates havoc in parts of Nigeria will presumably be controlled as good wells come into use and human trypanosomiasis will not be a problem so long as anti-tsetse measures are maintained. Mosquito breeding is mentioned but not discussed.

[The Anchan settlement is the biggest concentration of population yet made in Africa, and offers, perhaps the best opportunity for introducing to the African a mode of life far more beneficial than anything he has yet known but it seems evident that supervision will be needed for many years to expect of the African a rapid abandonment of conservatism would be unwise. It is necessary to take a long view.]

Charles Wilcocks

CLARKE J. D. Pattern for Progress in Rural Africa. Overseas Education 1948  
Apr. 17 No 3 295-301

This account of the Anchan Corridor gives much the same information as is given by McLEITCH (above) but adds emphasis on some of the points. The author notes with approval the fact that when the scheme was first mooted as a measure of control of trypanosomiasis the medical authorities were not content that it should merely offer protection against that disease, but decided, in collaboration with other departments that the whole area should be developed in the economic and social sense and that an advanced degree of rural hygiene should be encouraged. The population aimed at was not less than 70 to the square mile at which communal clearing is possible.

The new villages are now most attractive and people from outside the area apply to be allowed to settle in them. In these rural schemes there has been a mixture of compulsion and persuasion. In the opinion of the Control Officers the people appreciate the new way of life, but need supervision to ensure that the present high standards are maintained. One of the most important activities is the education of the people themselves, in the small schools which have been instituted. This is not education reserved for the few who show promise but simple instruction for the many, who may because of it be influenced towards the desire for better conditions than they have demanded in the past.

So far the scheme has cost £15 000 per annum which represents 5s per head of the population affected. The maintenance cost will now be reduced to one-fifth of these figures. Such expenditure is obviously worth while in terms of the health and welfare of the people. Anchau is not merely a method which ought to be widely used in the control of endemic disease. It is an example to all departments of government.

The author was cheered by the sight of a job well done. It was refreshing to visit a scheme which has been carried out without counting the pence and which has therefore been a success.

Charles H. Ilcocks

AUGUSTINE D. L. Some Factors in the Defense Mechanism against Reinfection with *Trypanosoma lewisi*. Reprinted from *Proc Amer Acad of Arts & Sciences* 1943 May v 75 No 3 85-93 5 figs on 1 pl [10 refs]

The author has studied the mechanism of immunity of rats to reinfection with *Trypanosoma lewisi* by examining the peritoneal fluid, the lymph nodes which drain this fluid, and the blood after intraperitoneal inoculation of large numbers (200-900 million) of trypanosomes. It was demonstrated that the trypanosomes passed as readily through the lymph nodes to the blood in rats which had recovered from a previous infection as in rats which had had no previous infection. In recovered rats however the trypanosomes arriving in the blood were rapidly removed within a few minutes to four days. The length of time of survival depends upon the titre of the antibody and the stage of development of the trypanosome in the blood. Dividing trypanosomes are almost immediately sensitized by the antibody being either killed or immobilized and are finally phagocytized by blood macrophages. Adult trypanosomes are more resistant and survive till the titre of the antibody reaches a point at which they are agglutinated into masses of living trypanosomes which are filtered from the blood in the internal organs where they are destroyed. The fact that the trypanosomes in the blood may commence dividing shows that any ablastin remaining from the first infection, which functions by stopping reproduction is inactive and plays no part in the immunity to reinfection. This immunity is dependent upon a humoral trypanocidal antibody to which developing parasites are particularly susceptible and adult parasites relatively resistant.

C. M. Wenyon

LAUNOY L. & LAGODSKY H. De l'action préventive d'une diamidine aromatique la diamidino-diphénoxypentane sur deux trypanosomoses expérimentales du rat. [The Preventive Action of an Aromatic Diamidine (Diamidino-diphénoxypentane) on Two Experimental Trypanosome Infections in Rats.] *Bull Soc Path Exot* 1946 v 39 No. 5/6 160-67

LAUNOY L. & LAGODSKY H. Nouvelle contribution à l'étude de l'action préventive de la diamidino-diphénoxypentane sur les infections expérimentales à *T. brucei* et à *T. evansi* du rat et du lapin. [Observations on the Preventive Action of Diamidino-diphénoxypentane on Experimental Infections with *T. brucei* and *T. evansi* in Rats and Rabbits.] *Bull Soc Path Exot* 1946 v 39 No. 5/6 197-200

SCHATZ A. MAGNUSON H. J. WAKSMAN S. A. & EAGLE H. Isolation of an Antibiotic Agent derived from a *Phycomyces* Active *in vitro* against *Trypanosoma equiperdum*. *Proc Soc Exper Biol & Med* 1946 June v 62 No 2 143-5

Several soil fungi have been found to produce filtrates active against *Trypanosoma equiperdum*. From a *Phycomyces* sp. a lipid-like substance was

isolated which immobilized the trypanosome *in vitro* but exerted no protective action against the experimental infection in mice.

No inhibitive agent has heretofore been obtained from this group of fungi. The selective action of the phycomyces factor against the trypanosome but not against bacteria, is of particular interest.

LYOFF M. Mims & NICOLLE, P. Recherches sur la nutrition des réductifs hémophages. V. Alimentation de *Trypanosoma infestans* Klug à l'aide de sérum vitamé. Importance de l'acide pantothénique. [Studies on the Nutrition of Blood-sucking Reductifæ. V. Feeding of *Trypanosoma infestans* by means of Vitaminized Serum. Importance of Pantothenic Acid.] *Bull Soc Path Exot* 1946, v. 39 Nos. 5-6 206-21 9 figs. [18 refs.]

DAVIS D. J. & SULLIVAN Thelma de S. Complement Fixation Tests for American Trypanosomiasis in Texas. *Pub Health Rep* Wash. 1946 July 19 v. 61 No. 29 1083-4

Complement fixation tests, in which *T. cruzi* antigen was used, were carried out on (1) 1,909 samples of serum, of which 568 were from persons who lived largely in shelters harbouring triatomid bugs (2) 1,002 Kline-negative samples chiefly from counties where *T. cruzi* had been demonstrated in insects and (3) 339 samples which had been negative to ordinary routine clinical diagnostic tests.

The only serum found to fix complement in a significant dilution was from an 8-year-old boy living in a neighbourhood where many specimens of *Triatoma gerstaeckeri* had been found to be infected with *T. cruzi*. No further evidence that he was infected was obtained by clinical examination or animal inoculation.

H. J. O'D. Burke-Gaffney

DUBOIS C. Chimiothérapie des trypanosomiasés.

This book is reviewed on p. 1087

## LEISHMANIASIS

NÁJERA ANGULO L. Hallazgo de *Phlebotomus* en Galicia y consideraciones sobre la epidemiología de las leishmaniasis. [Finding of *Phlebotomus* in Galicia. Epidemiology of Leishmaniasis.] Reprinted from *Boletín de la Real Soc Española Hist. Nat.* Madrid. 1945 v. 43 25-30 2 figs.

The author discusses the distribution of sandflies in the various provinces of Spain in relation to the existence of leishmaniasis visceral or cutaneous. He shows that recent observations have disclosed sandflies, chiefly *Phlebotomus perniciosus* in certain provinces even to a height of 1,500 metres, where their presence was previously unrecorded. These observations reduce the number of provinces in which both sandflies and leishmaniasis have not been demonstrated and it seems probable that careful observations by both clinicians and entomologists will fill the lacunae. The author shows in a map how close is the correspondence between the distribution of sandflies and leishmaniasis.

C. M. Wesson

AKALIN M. S. Anadolu Flebotomları. [*Phlebotomus* in Anatolia.] *Türkische Ztschr. f. Hyg. u. Exper. Biol.* Ankara 1941 v. 2 No. 2, 113-26 4 figs. German summary 127

The following species were found —*P. papatasi*, *P. perniciosus*, *P. minutus* and *P. sergenti*.

# *Leishmaniasis*

Vol. 43 No 11]

PACKCHANIAX A. The Distribution of Species of Sandflies, Genus *Phlebotomus* in the United States and their relation to the Transmission of Leishmaniasis. Texas Reports on Biol & Med 1946 v 4 No 1 35-41 [21 refs.]

NÁJERA ÁNGULO L. La existencia de lesiones cutáneas en la leishmaniosis visceral mediterránea y su significación epidemiológica. [Epidemiological Significance of Cutaneous Lesions in Kala Azar] Reprinted from Rev Clin Española 1945 Jul 15 v 18 No 1 28-37 4 figs. (12 refs) French summary.

Having encountered a case of kala azar in Spain in a boy who was suffering at the same time from ulcers on the lower lip and leg (in which however leishmania could not be demonstrated) the author discusses the world distribution of kala azar with particular reference to the disease as seen in Southern Asia and the Mediterranean region. He believes that from the point of view of the tendency to cutaneous ulceration and other lesions of other specific characteristics and of the co-existence of canine kala azar this area is divisible into three zones separated by a line running from a point just west of the Crimea and crossing the Mediterranean. It is not always easy to see on what grounds the conclusions are based nor the reason for introducing the subject of oriental sore which is discussed to some extent. The author's view is that knowledge of these subjects is most imperfect and that it is of the utmost importance that there should be carried out a co-ordinated investigation in the three zones centred on Pasteur Institutes in Algiers Athens and Baku.

C M Wenyon

PETRO H. Notícia acerca de 40 casos de kala-azar registados da consulta do pósto anti-seronótico do Poelinho em 1943 [Forty Cases of Kala Azar found by the Anti Malarial Organization at Poelinho Portugal, in 1943.] Seronismo Lisbon. 1944 (Trabalhos originaes-1943) 43-5

NÁJERA ÁNGULO L. Criterio diagnóstico en la leishmaniosis visceral mediterránea. [Diagnosis of Mediterranean Kala Azar] 52 pp 18 figs. [Bibliography] 1946 Madrid.

In this article the author discusses the various procedures and techniques which have been employed in the diagnosis of kala azar basing his remarks on cases of the infantile disease seen by him in Spain. He concludes that the only reliable criterion is the discovery of the parasite itself by puncture of a lymphatic gland the bone marrow or the spleen the operations are carried out in this order the later ones being undertaken only when the earlier ones have failed. He again refers to the presence of his supposed schizogony forms of the parasite in the bone marrow believing that the leishmania in other situations are merely phagocytosed organisms destined to destruction. Actually the article gives no new information of importance.

C M Wenyon

COOPER G R., REIN C. R. & BEARD J W. Electrophoretic Analysis of Kala-azar Human Serum. Hypergammaglobulinemia associated with Seronegative Reactions for Syphilis. Proc. Soc. Exper Biol & Med 1946 Feb v 61 No 2, 179-83 1 fig [27 refs.]

The electrophoretic patterns of 2 human kala-azar sera revealed the presence in high concentration of a unique abnormal component migrating with the  $\gamma$  globulin of the slowest mobility. The kala-azar sera, negative to serological tests



for syphilis provide instances which show that the presence of hyperproteinemia, hyperglobulinemia or hypergammaglobulinemia cannot be used to prove or disprove the specificity of positive serologic reactions for syphilis.

SAGHER, F. Activation of an Originally Negative Intracutaneous Leishmania Vaccine Reaction. *Acta Med Orientalia (Palestine & Near East Med. J.)* 1946 Mar v 5 No 3 82-5 2 figs.

In the vast majority of cases of cutaneous leishmaniasis, as shown by DOSTROVSKY the injection into the skin of a leishmania vaccine containing 100 000 culture forms of the parasite in 0.1 cc. is followed by a positive reaction characterized by redness over an area 3 cc. in diameter and a central papule. In certain cases which show little tendency to spontaneous healing and which prove very resistant to treatment the reaction is negative. These are often relapse cases, in which a lupus-like condition commences in the margins of an apparently healed sore. In a case described in this paper practically the whole of the right cheek became involved. Treatment by X-rays on a number of occasions failed to induce healing. The skin reaction at this time was negative to vaccines prepared from Palestine and Baghdad strains of leishmania. Treatment with Grenz-ray was then given, with the result that healing commenced. At the same time the skin reaction became slightly positive. Complete cure eventually resulted after a period of three years. When healing was complete the skin reaction was strongly positive to both vaccines. The author considers it possible that the failure of such cases as the one described, to show any tendency to spontaneous recovery is due to lack of development of antibody and that it is the lack of this antibody which causes the skin reaction to be negative. With development of antibody healing commences and the reaction becomes positive. On the other hand, the reaction may be due to an increased allergy or hypersensitivity having no relation to immunity. In either case it is not clear how the institution of treatment by Grenz-ray could bring this about.

C. M. Wemyss

BOSE, A. N., GHOSH, T. N., MITRA, S. V. & DATTA, S. On the Toxicity of some Organic Antimonial Drugs used for the Treatment of Kala Azar. *Indian Med. Gaz.* 1946, Jan. v 81 No 1 13-18.

It is well known that organic antimonials employed in the treatment of kala azar vary considerably in toxicity from batch to batch. This is particularly the case with derivatives of  $\beta$ -aminophenylstibonic acid such as urea stibamine (the exact composition of which is still uncertain) the diethylamine salt (neostibosan) the triisopropylamine salt and others. With a view to throwing light on these variations in toxicity a number of different batches of these preparations were studied from the point of view of their total antimony content and the various combinations in which this antimony was present. At the same time toxicity tests were carried out in mice. It was found that though the toxicity of urea stibamine generally increased with a rising antimony content, it was clear that this was not the sole cause as certain samples with high antimony content were less toxic than others with a lower content. An explanation was found in the presence of antimonious acid. If the ratio of antimony present as antimonious acid to that present in pentavalent organic combination exceeds 1:26 there occurs a definite increase in toxicity. If care is taken, in the preparation of urea stibamine to keep the ratio low it will satisfy much higher toxicity limits than those at present accepted (namely 200-225 mgm./kgm. intravenously). As regards the other compounds studied, the di-ethylamine, and the iso-propylamine salts, their toxicity depends largely

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on impurities in the amines employed in their preparation There was also some indication that the toxicity of the di-ethylamine salt could be reduced by incorporating a minute trace of a suitable reducing agent

C M Henson

DUTTA, N K MUKERJI B & SEKAR C C The Possibility of using Pigeons in Toxicity Determinations of Organic Antimony Compounds. *Quart J Pharm & Pharmacol* 1946 Apr-June v 19 No 2 89-96 2 figs

Since white rats and mice are not freely available in all parts of India the use of pigeons has been suggested for determining the toxicity of organic compounds of arsenic and antimony. The common Indian pigeon (*Columba livia intermedia*) is found all over the country and can be obtained at reasonable cost. It is easily handled and is not exacting in its requirements. These birds kept under good conditions in groups of four were used in conjunction with chemical tests for the assay of urea stibamine. A freshly prepared 4 per cent aqueous solution was given into a wing vein. Not less than twenty pigeons were inoculated at a time and the period of observation was one week. For the purpose of comparison parallel toxicity tests on the same batch of drug were carried out with mice. From analysis of the results obtained in the two series of tests it was concluded that under the conditions employed the use of pigeons for bio-assay was justified

J D Fulton

OASTLER E. G & FIDLER H. K. Cerebral Lesions produced in Healthy Dogs by the Intravenous Injection of 4,4-Diamidino Stilbene. *Trans Roy Soc Trop Med & Hyg* 1946 June v 39 No 6 533-8 5 figs. (4 on 1 pl.)

In this paper are described certain lesions of the central nervous systems in dogs following the intravenous injection of freshly prepared solutions of stilbamidine. The experiments were undertaken because of observations made on cases of kala azar treated with old solutions of stilbamidine which had been exposed to light. A number of dogs treated with the same old solutions showed pathological lesions in liver and kidneys. It is now well known that under the above conditions stilbamidine solutions undergo photochemical change [this *Bulletin* 1943 v 40 23 683 684 1944 v 41 196 1945 v 42 18]. When freshly prepared solutions were administered to 10 other dogs significant pathological lesions occurred only in the c.n.s. and were associated with definite clinical signs especially spasticity. The lesions described in the text included infiltration and thickening of the walls of blood vessels myelin degeneration softening inflammation have previously been described in and thrombosis. Nervous disturbances of the diamidine series [this *Bulletin* 1940 v 37 404 1942 v 39 748 1944 v 41 273]. The dosage schedule for man and animals treated with members of the diamidine series was 1 to 21 mgm. per kilo. of body weight given intravenously each day during the first second and third weeks respectively. From 4 to 21 of them showed clinical signs indicative of damage to the c.n.s. which was verified *post mortem* but its degree was apparently unrelated to the amount of drug given. Three other animals had no brain lesions while in the remaining two the damage was microscopic. Foci of necrosis occurred in the liver of one dog, and others had slight fatty degeneration of the kidneys. The cerebral lesions were believed to result from vascular spasm or anoxia and in view of the neuropathic signs noted in human cases after treatment with diamidines this probably does not represent a special susceptibility in the case of dogs.

J D Fulton

MUKERJEE S. Penicillin for Isolation of Bacteria Free Culture of *Leishmania* Parasites. *Ann Biochem & Exper Med Calcutta*. 1945 v 5 No. 3 95-6

The author has shown that the flagellates in cultures of *Leishmania*, both in liquid and on solid blood media are highly resistant to penicillin though with increase in the concentration of penicillin from 100 to 1,000 units per cc. a decreasing percentage of flagellates survive. Nevertheless the surviving flagellates in the media containing the highest concentration of penicillin are able to give rich cultures when introduced into penicillin-free media. Advantage is taken of this resistance to penicillin in the isolation of *Leishmania tropica* from contaminated skin lesions. The contaminated material from the lesion is inoculated into liquid or solid medium containing penicillin (200 to 1,000 units per cc.) After a few days incubation at 22°C. subculture into penicillin free medium is made or if staphylococci are still present once more in a penicillin medium.

C M Wenyon

DOSTROVSKY A. & SAGHER, F. Generalized Recurrence in Leishmaniasis (Oriental Sore). Report of a Case with 110 Lesions. *Ann Trop Med & Parasit* 1945 Oct 10 v 39 No 2 98-100 4 figs. on 1 pl.

The case described is that of a girl of 10 years of age from Aleppo who suffered from multiple skin lesions due to *Leishmania* infection. These lesions healed in four months, but about four months later fresh lesions began to develop at the original foci, and continued to do so till complete relapse of the original condition had occurred. In the course of time certain lesions showed a tendency to spread to new foci by way of the lymphatics. When the patient was seen by the authors after the disease had persisted for four years there were 110 lesions some of the larger of which were due to confluence of a number of smaller ones. The distribution was on the face and limbs including the gluteal region. Some were present also on the inner mucous surface of the lower lip. The lesions were of a lupoid, serpiginous, gummatous and ulcerative type. The diagnosis was established by the discovery of *Leishmania* in smears, and by culture from the lesions. The author concludes that in this case there had been a complete breakdown of the usual cutaneous immunity. As a rule, in the few cases which relapse, this is a local phenomenon involving only one or two of the many healed foci of infection.

C M Wenyon

PISSÓA, S. B. & BARRETO M. P. Contribuição para o estudo da imunidade da leishmaniose tegumentar americana [Immunity in S. American Cutaneous Leishmaniasis.] Reprinted from *1 Reunião Anual dos Dermatologistas Brasileiros Rio de Janeiro 28-29 Sept 1944* 1945 137-51 [28 refs]

In discussing immunity in S. American cutaneous leishmaniasis the authors show that after recovery the majority of infected individuals possess a solid immunity. Apart from the fact that as a rule secondary or relapse lesions do not develop this is supported by the negative Montenegro reaction and the failure to produce infection by inoculation of living cultures in recovered individuals. In some persons however at various times after healing of the primary sore secondary lesions appear on the skin or mucosae. These are the result of metastatic distribution of parasites which in certain cases, have been shown to survive even in the cicatrized lesions. Occasionally there exists a natural immunity as shown by one or two individuals of a family who alone

*Fevers of the Typhus Group*

fail to acquire the disease though they are as heavily exposed to infection for many years as other members who became infected. In some a very mild type develops illustrating a partial natural immunity.

Experiments on monkeys show that 100 per cent become infected from inoculation of living cultures. Vaccination of six monkeys with a vaccine of killed flagellates protected four against infection with subsequently inoculated living flagellates. When these experiments were extended to human beings of 444 vaccinated individuals 12 (2.7 per cent) subsequently acquired the disease in an endemic focus while of 683 unvaccinated individuals 108 (15.6 per cent) became infected in the same period. In the vaccinated individuals who were immune the Montenegro reaction was negative as in the case of persons who were immune after recovery from the naturally acquired disease. It is concluded that vaccination can play an important part in the prophylaxis of American cutaneous leishmaniasis.

C M Wenyon

## FEVERS OF THE TYPHUS GROUP

ANIGSTEIN, L. Problems of Nomenclature of certain Pathogenic Rickettsiae and Rickettsial Diseases. *Texas Reports on Biol & Med* 1946, 4, No 2 111-18. [12 refs]

The author stresses the need for an agreed nomenclature of the pathogenic rickettsiae and of the diseases caused by them. He mentions some of the attempts that have been made to formulate a satisfactory nomenclature and makes a proposal that a technical Inter American committee should be set up to make recommendations on the subject in accordance with the accepted international rules of botanical nomenclature. He rightly lays emphasis on the importance of simplicity and usefulness in connexion with the choice of names. He admits that the knowledge of the biological properties of the rickettsiae is incomplete and that no final judgment can yet be passed on the exact position of the pathogenic rickettsiae in the system of microbiology. He states that only one of the many names applied to these organisms has received universal acceptance, viz *Rickettsia prowazeki* Rocha Lima, 1916. He favours the use of the following names: Louse-borne typhus fever *fele-boroe* typhus fever, Rocky Mountain spotted fever *Dermacentor* *tsutsugamushi* Wolbach 1919 *tsutsugamushi* disease and *Rickettsia tsutsugamushi* Hayashi 1920 but does not express a dogmatic opinion regarding the most suitable names for the organisms causing flea-borne typhus and bontonneuse fever.

[A generally accepted nomenclature for the fevers of the typhus group and their causative organisms is badly needed but a committee attempting to deal with the matter would encounter a serious difficulty at the very outset. A primary requirement of scientific nomenclature is that each name must apply to something that can be clearly identified and differentiated from all other objects or conditions. Seeing that pronounced differences of opinion still exist among experts with regard to the relationships of the different fevers of the typhus group it seems necessary to fall back on provisional names which

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C. M. Wenyon

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ought to convey helpful suggestions of the chief features of the diseases in so far as these are known at the present time.

Two of the names considered most suitable by the author—louse-borne typhus and flea-borne typhus—comply with these requirements and there seems to be no valid objection to the extension of the same type of nomenclature to the mite-borne and tick-borne fevers of the group. Clinically and pathologically, these diseases are generally agreed to be closely related to classical typhus, and their association with mites and ticks is universally recognized.

Some workers believe that there are two or more tick-borne typhus fevers, so it would be desirable to add the name of the locality of occurrence or of the type of the disease (Rocky Mountain, boutonneuse etc.)

Each of the causative organisms of the different typhus fevers could be referred to as the rickettsia of the fever concerned.

The use of this system of nomenclature would not imply adhesion to one or other of the conflicting views regarding the antigenic relationships of the causative organisms. The name typhus fever of unknown or doubtful vector would cover the cases in which no satisfactory evidence can be obtained to incriminate any one vector and in such cases the addition of the name of the serological type (O119 OLA OVS or indeterminate) would be helpful.

In the interests of brevity the word "bore" could be dropped without fear of causing misunderstanding.

The rules of botanical nomenclature are not applicable to the names of diseases, and the time is not ripe for a final pronouncement on the names of the rickettsiae of the typhus fevers.]

John W D Megaw

MACCHIARELLO A CUEVISTAS T O & OVALLE H Estudios sobre tifo exantemático 1. Influencia de la administración parenteral de altas dosis de ácido ascórbico en la evolución del tifo Europeo (no orquítico) experimental del cobayo. (The Effect of Parenteral Administration of Large Doses of Ascorbic Acid on the Evolution of Experimental European (Non-Orchitic) Typhus in Guinea-pigs.) Rev Chilena de Hig y Med. Preventiva 1945 Sept v 7 No. 3 175-87 1 fig [11 refs.] English summary

The authors report the results of experiments designed to show whether large doses of vitamin C have a preventive or curative action in guinea-pigs infected with typhus rickettsiae.

Ten guinea-pigs were given daily doses of ascorbic acid ranging from 50 to 1000 mgm by subcutaneous or intramuscular injection, starting from the day on which they were inoculated with epidemic typhus rickettsiae. These animals, and 15 controls infected in the same way were given the usual vegetable diet. The effects observed are described in detail. They can be summarized as follows—(1) pronounced, but temporary antipyretic action proportional to the doses given (2) diminution in the number of brain nodules (3) a tonic action shown by hypothermia, or even death (4) an absence of anti-rickettsial action, as shown by the normal duration of the incubation period the return of the fever curve to the usual type after cessation of the injections and the retention of the virulence of the infecting rickettsiae.

It is also pointed out that in Chile the morbidity of typhus fever is highest during the spring and summer when the diet of the people is richest in vitamin C.

John W D Megaw

## Fever of the Typhus Group

MACCHIARELLO A CUFUENTES O & OVALLE H Estudios sobre tifo exantemático VI Influencia de la vitamina C sobre la evolución de la curva en el tifo exantemático humano y experimental del cobayo [The Effect of Vitamin C on the Fever Curve of Exanthematic Typhus in Man and Experimental Guinea-pigs.] *Rev Chilena de Hig y Med Preventiva* 1945 Sept v 7 No 3 189-86 1 fig English summary

Eight guinea-pigs were given daily subcutaneous injections of ascorbic acid in doses of 100 to 1 000 mgm starting from the first day of fever resulting from inoculation with epidemic typhus rickettsiae. The effects were similar to those described in the preceding paper except that the typhus nodules were more abundant. The two guinea-pigs that received doses of 1 000 mgm died after two and six days and no cause of death other than the toxic action of the drug could be detected.

Intravenous injections of ascorbic acid were given to 23 epidemic typhus patients in daily doses of 100 to 600 mgm. The average response was a fall of the temperature by 0.5 to 1.0°C. In a quarter of the cases the duration of the fever was reduced to 10-12 days and in one-third of the patients there was an apparent improvement in the general condition but there were five deaths including two in cases in which the treatment had been started on the 3rd and 5th days.

The action of the drug was regarded as being similar to that of any effective antipyretic. In one case rickettsiae were isolated from the patient's blood after the temperature had fallen to normal.

John W D Megaw

MACCHIARELLO A & OVALLE H Estudios sobre tifo exantemático VII Estudio experimental acerca de la acción *in vitro* del ácido ascórbico sobre el virus del tifo exantemático epidémico (Europeo) [An Experimental Study of the Action *In Vitro* of Ascorbic Acid on the Rickettsiae of Epidemic Typhus (European)] *Rev Chilena de Hig y Med Preventiva* 1945 Sept. v 7 No 3 197-209 1 fig English summary

In a series of controlled experiments various suspensions containing the rickettsiae of epidemic typhus were kept in contact with acid and neutral solutions of ascorbic acid for 5 to 15 minutes at a temperature of 37°C and then used to inoculate guinea-pigs. The only inhibiting effects observed were with the acid suspensions and it was concluded that the acidity of the inoculum was responsible for these so that there was no evidence of any anti-rickettsial action *in vitro* by vitamin C. Even if there should have been any anti-rickettsial action this must have been transitory and reversible it did not affect the viability or virulence of the organisms. For details of the experiments the original paper must be consulted.

John W D Megaw

DAVIS D E & POLLARD M Prevalence of Typhus Complement Fixing Antibodies in Human Serum in San Antonio, Tex. *Pub Health Rep Wash* 1946 June 21 v 61 No 25 923-31

The authors carried out complement fixation tests on the sera of 4,219 persons engaged in food-handling in San Antonio Texas. Wassermann positive sera were excluded to avoid the possible fallacy due to false positive reactions. The antigen was prepared from the Wilmington strain of murine rickettsiae. Complete fixation with serum diluted 1-10 was regarded as indicating the occurrence at some earlier date of an attack of murine typhus.



[November 1946]

The percentages of positive reactions in the various groups of persons tested are shown in the table

	Number tested	Percentage found positive
Whites—Male	662	2.3
	1,035	3.0
Latin American—Male	920	5.0
	1,540	3.2
Negroes—Male	114	4.3
	218	4.1
Total	4,218	3.5

Although the authors admit that the persons tested were specially exposed to risk because of their occupation the results are regarded as showing that many cases of murine typhus had not been reported, presumably because they were sub-clinical.

John W. D. Meyer

McCulloch R. N. Studies in the Control of Scrub Typhus. Med. J. Australia. 1948 May 25 v. 1 No. 21 717-38 14 figs. (Numerous refs.)

This paper consists for the most part of a report on the introduction and practical application of dibutyl phthalate as a method of controlling scrub typhus among the Australian troops in the recent war. At the end of 1942 information was received from the U.S.A. that dimethyl phthalate was of special value in protecting against the bites of larval mites when applied to half inch bands to all entrances to clothing and to wider bands on the socks. The author who was appointed to study the methods started work at Sydney in March 1943 and continued his investigations in South Australia, Queensland, New Guinea and Borneo.

In early experiments it was found when dimethyl phthalate was rubbed on the clothing using 1.0 to 1.25 cc. for each square foot, bites were prevented for two days but that application in bands four inches wide, using 3.5 cc. per square foot to all entrances to the clothing failed to give protection against bites. The chemical appeared to act by poisoning rather than by repelling the mites which travelled freely on the treated clothing but died after about an hour's contact.

Dibutyl phthalate was found by test to be even more effective and as it could be made available in larger quantities it was used in the further tests. DDT had also been tested but sets of clothing treated by sprinkling with four ounces of petrol or six ounces of kerosene containing 5.0 gm. in solution, or by dusting with 7.5 gm. of the powder ceased to be protective after the clothes had been washed four times in soap and running water whereas one ounce of dibutyl phthalate rubbed into the clothing remained protective after eight washings in the same way.

The efficacy of various methods of treating cloth was tested by applying the larval mites to squares of the treated fabric mounted on three-ply boards and finding the time that elapsed before the mites ceased to move. Full details are given of numerous experiments. In New Guinea it was found that when larvae of *Schöngastia blattarum* or *S. pusilla* were applied to cloth treated with

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dibutyl phthalate at a rate corresponding to one ounce for each set of field clothing all movement was arrested within a maximum period of about half an hour even after the cloth had been washed up to eight times with soap and running water in the manner available to troops in the field. The results were equally satisfactory whether the application was made by hand rubbing or by sprinkling with emulsions or with mixtures of the chemical and alcohol Laundry washing involving two periods of washing for ten minutes with soap solution at 135°F and three machine rinsings totalling 15 minutes caused an appreciable diminution in the toxic effect so that clothing washed twice in this way was no longer protective. These tests were made with cotton clothing woollen cloth treated in the same way ceased to be protective after three to seven washings in soap and running water when vigorous rubbing formed part of the procedure but when the orthodox method of squeezing was employed the protective effect persisted as well as it did in the case of cotton cloth.

In the numerous conditions in which the tests were carried out there was no evidence of a breakdown in the protection afforded except in the case of woollen socks for which more frequent treatments were found desirable.

In some of the tests a few larvae of *Schöngastia parva* *Trombicula minor* *T. Fletcheri* (now regarded as a synonym of *T. akamushi*) and *T. halorisi* were included all of these seemed to be fully susceptible but some species of *Guntherana* and *Aconitacarus* remained active twice as long.

In tests carried out in Queensland *T. minor* was found capable of prolonged survival on treated fabrics after four or five washings.

The standard method of treating service clothing in field conditions was to supply each man with one ounce of dibutyl phthalate for each set of clothing. The fluid was poured into an open tin a little at a time was taken up by the finger tips of one hand spread over the palmar surfaces of both hands and smeared on the clothing. About 75 applications of this kind could be made from one ounce in such a way as to make a light uniform smear over the shirt trousers and socks. Fortnightly treatments were regarded as affording reliable protection even in severe conditions of wetting with rain and sweat and the protection persisted after washing six or seven times with soap and water. Treated clothing if stored unused and without washing remained fully protective for at least two months.

The fluid was not irritating to the skin except over the scrotum even when applied directly but when it was used as a mosquito repellent great care had to be taken to prevent entry into the eyes.

In some cases it was found advisable to treat the socks once a week. Blankets were treated in the same way once every six months one ounce and a-half was enough for each article.

Benzyl benzoate stated in U.S.A. confidential reports to be an outstanding miticide when applied to clothing was not available for testing. Dimethyl phthalate though more rapidly toxic than dimethyl phthalate to larval mites when applied to clothing not afterwards washed ceased to be protective after one to three washings. Two American mosquito repellents, Staway and Rutgers 612 were found highly protective but ceased to be effective after washing.

Statistics are given to show the striking reduction in the incidence of scrub typhus that resulted from the systematic adoption of the treatment of clothing. In cases of apparent failure it was almost always found that the substance had not been properly applied. Almost complete control of scrub itch was also obtained.

Some notes are given on the habits of larval mites. The most rapid rate of travel on cloth was about 1 in. in four seconds. Boot collecting, though

## PLAGUE.

DAVIS D H S Plague in Ngamiland, Bechuanaland Protectorate. Union of South Africa Ann Rep Dept Public Health Year ended 30th June 1945 51-2

In this abbreviated report on the survey, of Ngamiland many interesting points of plague epidemiology are raised and illustrated. As an epidemic of plague it was the largest outbreak in Southern Africa on record and furnished 304 total cases with 158 deaths. The true mortality however was probably nearer 60 than 50 per cent. It began with the notification in the first week of October 1944 of a number of sudden deaths in a population of 15 000 persons. Recognition of the nature of the disease was soon forthcoming and measures were hurriedly adopted to deal with prevention of spread. These were — anti-plague vaccination (presumably with a killed vaccine) recruitment of an anti-rodent staff to engage in bait-spraying application of cyanogen and destruction of vermin quarantine of areas concerned and prohibition of inter-kraal movement. Most of the cases were bubonic but some invariably fatal were septicaemic or pneumonic. There was no doubt that the insect vectors were plague-infected fleas, and most of these were without rodent hosts for much of the epidemic. Moreover this epidemic has the added interest of the data which are now accumulating on the survival time and transmission potentiality of the plague flea. This fact has special significance in view of showing the connexion not only of epidemic with epizootic but also of epidemic with syphatic plague. The rodent concerned, the multimammate mouse belongs to the class of the semi domestic mice. There was an unusually favourable season for increase in the population of these small rodents, which synchronized with the peak of a secondary plague epizootic in them (from a primary epizootic in gerbils) and with flooding of swamp rodent burrows. The consequent over-crowding of the mice and food shortage sent the rodent population to the human habitations the villages and kraals, to get grain and other food. With the onset of warmer weather in September and October climatic conditions for the spread of plague from infected rodent fleas to man became more favourable and the human epidemic resulted. A series of recommendations applicable to the primitively housed population of Ngamiland, are given and special note is made of the great possibilities of DDT for the control of insect-borne diseases in such a population.

W F Harvey

BLANC G & BALTARARD M Virulence des déjections de puces pesteuses. [Virulences of Plague-Flea Dejects.] Ann. Inst. Pasteur 1948 May-June '72 Nos 5/8 499-9 1 fig

Originally several thousand fleas were fed on plague-infected guinea-pigs and once these fleas were definitely infected they were placed in a flea-house to which only fresh fleas were afterwards added. These fresh fleas usually became infected by the second day. Breeding took place and litters of new fleas became infected on the animals contaminated by their predecessors. The process had gone on for 14 years when flea dejects were removed, for the purpose of these experiments from the hair of a white rat which had been placed in the flea-house. This rat was dead by the following evening of proved plague. The dejects were sealed in an ampoule and kept in the dark at room temperature. Tests of this material by subcutaneous inoculation of guinea-pigs proved that it was still capable of causing plague after 24 hours 122 days 180 days 316 days 1 year and 18 months. The significance of these experiments is obvious. It would seem probable that the virulence of dejects in burrows can be long maintained.

and that this would suffice to provide one explanation of the endemicity of plague in rodents. Still further deductions are permissible which would extend infectivity via the faeces not only to the human flea but also to the louse especially as it has been shown that mice can be infected through mucous membranes by dejecta of *Pulex irritans* from human plague habitations.

W F Harvey

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

WATSON J M The Effect of Urine on *Entamoeba histolytica* Ann Trop Med & Parasit 1945 Oct 10 v 39 No 2, 101-16 1 fig [31 refs.]

The author has investigated the action of urine on *E. histolytica* from the point of view of the possibilities of urinary amoebiasis. He has shown that at the temperature of the human body urine is highly lethal to the amoebae which are quite unable to live in it. The lethal effect however develops slowly the first signs being noticeable in two hours. Exposure to urine of various concentrations either alone or mixed with faeces at lower temperatures for periods exceeding two or three hours results in a gradual reduction in the numbers of amoebae and loss of motility in those that remain. After 24 hours the majority of the amoebae are degenerate and quite unrecognizable. These results emphasize anew the well known rule that in the collection of faecal samples for diagnosis of amoebic infection it is imperative to avoid admixture with urine. Tests were carried out in order to discover the cause of this lethal action. The amoebae were shown to be capable of surviving and multiplying in media with a pH as low as 5.9 while they remain uninjured by still lower pH values for several hours. As regards osmotic pressure the amoebae can live in solutions equivalent to Ringer's solution of from 0.3 to 1.7 times the normal strength. Quite apart from the lethal action of variations in pH or osmotic pressure urine may be toxic on account of two of its constituents namely urea and ammonia both of which killed and disintegrated all amoebae in culture tubes in 48 hours.

From the results of his experiments the author concludes that it must be extremely difficult for *E. histolytica* to establish itself in any part of the urinary tract where it will be continuously immersed in urine. On the other hand, amoebic invasion of the walls of the urinary passages by direct or metastatic extension might occur in such a manner that the amoebae in the wall were not continuously bathed in urine. From such lesions amoebae might from time to time escape into the urinary passages and if rapidly voided before degeneration occurred, give rise to a diagnosis of urinary amoebiasis. Actually however there is no information available regarding the condition of the walls of the urinary passages in the few cases of urinary amoebiasis which appear to be authenticated. [See also the critical review of urinary amoebiasis by the same author this Bulletin 1945 v 42 947]

C M Wenyon

SNELL, A. M. Some Clinical Problems of Amoebiasis. U.S. Nav Med Bull 1946 July v 46 No 7 1023-40 2 figs [18 refs.]

The author has written this paper in view of the increased occurrence of amoebiasis in the United States as a result of the return there of men infected overseas. Whilst it contains nothing original the paper consists for the most part of a well-balanced appreciation of the epidemiology pathology clinical picture complications and sequelae diagnosis and treatment

[November 1946]

of amoebiasis. The fundamental diagnosis of the condition by finding the parasite is suitably stressed and the need for tenacity of purpose and for skill in the procedure is mentioned. The ancillary methods of examination are discussed in proper perspective. The remainder of the paper contains brief accounts of four cases of amoebiasis illustrative either of its main features or of the difficulties in its diagnosis when associated with complicating diseases.

A R D Adams.

[In the reviewer's opinion this paper is an admirable and up-to-date general account of amoebiasis worthy of wide circulation]

Proc Roy Soc Med 1946 July v 39 No 9 541-60 (Sect. of Proctology 9-18) Discussion on the Use of Medicaments in Diseases of the Colon and Rectum. MURGATROYD F HARGREAVES W H LOVIBOND J L SOMERVILL T H MORGAN C N WRIGHT A D HUNT A H]

Opening the discussion MURGATROYD stated that the drugs commonly used in the treatment of amoebiasis fall into three groups—(1) Ipecacuanha derivatives (emetine hydrochloride and emetine-bismuth-iodide) (2) substituted phenyl arsonates (carbarsone and stovarsol) and (3) iodoxyquinoline compounds (chimofoin and doodoquin). After brief consideration of the treatment in vogue for amoebiasis he stated that the successes achieved had been variously assessed as between 75 and 95 per cent. To understand the failures it is necessary to consider the parasite the patient and the procedure. There is no sound experimental evidence that drug resistance is acquired by the parasite. Whether some amoebae live in the bowel as commensals, or whether all live in the tissues, has not been established. The state and distribution of the drugs in the body is a matter of speculation. The state and distribution parenterally is largely excreted in the urine, and fails to cure an E histolytica gut infection. In man it fails to sterilize most of the acute cases, and is particularly poor in this respect in producing cure and this may be due by its slower absorption by this route and the consequently longer maintenance of an amoebicidal concentration in the tissues. The control of a concomitant bacterial colitis may render an amoebic infection more amenable to successful treatment, but the primary aim should be to sterilize the amoebic infection before such a condition develops.

HARGREAVES spoke of the chronic bed-ridden cases of amoebiasis from Burma seen by him after they had received many emetine injections and other treatments, both overseas and at home. He found the outlook for these distressing cases considerably changed when penicillin was given as it rendered the amoebic dysentery more amenable to specific drugs. Its use with sulphasalicylate concurrently was therefore adopted for such cases, as a preliminary to a combined course of anti-amoebic treatment. Penicillin and sulpha-salicylate treatment was tried for chronic ulcerative colitis in nine cases with satisfactory immediate results, although permanent cures could not be claimed.

LOVIBOND reviewed his clinical impressions of about 1,000 hospital cases of amoebic dysentery in Ceylon, Assam and Burma, and concluded that a continuous sequence of treatment is all-important. EBI and chimofoin enemata are possibly the keystones of treatment and Carbarsone should clear residual cysts.

Howard SOMERVILL, recording his South Indian experience of colonic disease, said of amoebiasis that most of the work of the medical wards seemed to be "clearing up the failures of other doctors by giving continuous courses

of emetine to patients who had already had scores of injections but never more than five or six at one time. He stressed the importance of continuous daily treatment with E.B.I. for at least 12 days and the need for adjuvant treatment with quinoxyl retention enemata in chronic cases. He referred to 10 cases of amoebic disease of the rectum and four of amoebic abscess in the perineum and buttocks in which surgery and emetine treatment were effective. All cases of carcinoma of the rectum in the tropics should be examined for amoebae before operation or radium treatment. He related his experience with cases of concurrent bacillary and amoebic dysentery of bacillary dysentery and of tuberculous disease of the colon.

Naughton MORGAN spoke of the difficulties in differential diagnosis of amoebic tumours of the gut and the dangers of operation in undiagnosed amoebiasis or bacillary infection. In discussing the use of sulphasuxidine in the surgery of the rectum and colon he recommended bigger dosages prior to bowel surgery than those originally advocated by POTH.

Dickson WRIGHT listed a number of conditions, including amoebic dysentery which benefit from sterilization of the faeces by suitable sulphonamide therapy and HUNT recorded data showing the reduction in the incidence of peritonitis complicating major intraperitoneal surgery of the colon and rectum after pre-operative sulphasuxidine treatment. A R D Adams

RADNA, R. Sur le traitement de l'amoebiose par l'iodoforme (Deuxième note.) [The Treatment of Amoebiasis with Iodoform.] *Ann. Soc. Belge de Méd. Trop.* 1945 Dec 31 v 25 No 3/4 219-20

The author treated 18 carriers of cysts of *E. histolytica* with iodoform using the technique recommended by CASTELLANI and SCOTT. The iodoform was given in small gelatin capsules each contained in a much larger capsule of sodium bicarbonate.

Each capsule of iodoform contained 0.05 gm. One such capsule was given on the first day of treatment two on the second four on the third and six on the fourth day. The dose of six capsules was continued until the fourteenth day. A second course was given after a month's rest. For the two courses a total dosage of 7.3 gm. was thus administered. Twelve of the patients were free from cysts after 15 days of treatment and 16 after 1 month.

The author points out that the relatively low price of iodoform makes it possible to employ it on a large scale in the sterilization of carriers of *E. histolytica* cysts. H J O D Burke-Gaffney

BRUG S L. Pseudoparasitism of the Human Intestinal Tract. *J. Parasitology* 1946 June v 32 No 3 222-4 1 fig [14 refs.]

On one day in four out of thirteen fecal samples from a psychiatric ward, coccidial oöcysts, probably of *Eimeria debilis* were found. The cysts stained red with eosine solution and were apparently dead. Possibly they had been ingested with liver sausage for the preparation of which pigs' bowels may have been used.

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES.

D'IGNAZIO C. & CODELORCINI, E. La forma polmonitica della febbre ricorrente e la polmonite primitiva dermatofosa. Nota clinica. [Pneumonic Form of Relapsing Fever and of Typhus.] Boll. Soc. Ital. di Med. e Ig. Trop. (Ser. Entres) 1945 v. 5 Nos. 5/8 211-20 English summary (3 lines)

Details are given of four cases selected from a larger number. They are important to note because in all of them the symptoms pointed strongly to a lobar pneumonia of the ordinary pneumococcal type—pain, cough, fever, haemorrhagic sputum and signs of consolidation—but the basic disease was relapsing fever or typhus. Eighteen of the former are mentioned and 12 of the latter. The four detailed were sent to hospital as cases of frank pneumonia and it was the presence of an enlarged liver or spleen, and the failure of sulphonamide drugs to relieve which led to further laboratory examination and the finding of the spirochaete in the one type and of a positive Weil-Felix in high dilution (up to 1:2,560) in the other.

H Harold Scott

D'IGNAZIO C. Schemi di terapia delle febbri ricorrenti africane. [The Treatment of African Relapsing Fever.] Boll. Soc. Ital. di Med. e Ig. Trop. (Ser. Entres) 1945 v. 5 Nos. 5/8 17-27 English summary (2 lines)

The author gives his views on the treatment of relapsing fever in Addis Ababa, which is chiefly louse-borne. He uses neosalvarsan, bismuth and stovarsol. [The author refers to neosalvarsan and "salvarsan" indiscriminately.] In the early febrile stage he gives neosalvarsan in fairly large doses (0.6-0.75 gm.) intravenously with, or without, Hepatamin (presumably a liver preparation) as a protective and injected slowly. In the second attack of fever to forestall renal and hepatic lesions he gives first a small dose of 0.1 or 0.15 gm. neosalvarsan to test the patient's tolerance and then returns to the larger dose (0.6 gm.) After the crisis there may be no more attacks, but as a prophylactic 0.3 gm. may be given intravenously and repeated every 3-4 days for 3-4 times. When the patient has had 1.8-2.1 gm. in the first night after the attack, and there has been no relapse, he may be regarded as cured. The author is not an advocate of the still larger doses (0.6 gm.) as recommended by some physicians.

For treatment during the afebrile period the following course is favoured. If begun during the first three days of calm, injections of neosalvarsan should be made intramuscularly on alternate days in doses of 0.2 0.3 0.4 0.5 0.6 and 0.6 gm., the interval between the penultimate and the last dose being 3 days. If administered in the second 0-4 gm. repeating it twice on alternate days then larger initial dose is given [totalling says the author 2.1 gm. but as stated 0.5 gm. repeating thrice] (the total would be 3.2 gm. He is presumably referring to neosalvarsan, in view of the relatively high dose). Bismuth he uses in doses of 30-40 cgm. suspended in oil and injected intramuscularly. If desired, it may be given on the days intervening between those for injection of neosalvarsan. Stovarsol per os is useful for children. To the very young he gives 0.25-0.45 gm. daily for 10 or more days. For children "in the second infancy" (7-10 years) the dose is 0.5-0.7 gm. daily for the same length of time. For adults during the fever period he gives 1.25-1.5 gm. on two consecutive days and has obtained cure without further treatment. During the afebrile period he gives 0.75 gm. daily for 7-8 days and claims that he has usually obtained a cure by this means in exceptional cases a longer course is needed.

## Yaws

Patients presenting signs of hepatic inadequacy—jaundice epistaxis, petechiae with pain over the liver—are given 50-80 gm of glucose daily and 10-20 units of insulin subcutaneously. If the glucose causes vomiting when taken by mouth it may be given intravenously in 10 per cent. solution 10-20 cc. at a time. For headache the ordinary antineuralgics usually suffice but if it is very severe lumbar puncture may be needed [the quantity of fluid to be with drawn is not stated] for the rheumatic symptoms salicylates may be given by mouth by rectum or by injection and vitamin B intramuscularly or intravenously.

H Harold Scott

## YAWS

WINDELLE J H REIN C R STERNBERG T H & SHELDON A J Preliminary Report on the Evaluation of Penicillin in the Treatment of Yaws. *Amer J Trop Med* 1946 May v 26 No 3 311-18 1 graph. [10 refs.]

The authors review seven papers on the subject and find that although clinical cure of yaws has resulted even with small doses of penicillin (50 000 to 500 000 Oxford Units) very few cases were observed to attain Kahn or Wassermann sero-negativity.

The present work was done in a part of Haiti where syphilis was not prevalent. Three groups of patients were studied the details are set out in the Table below.

Approximately 60 per cent in each series were under 17 years of age. The diagnosis of yaws depended on clinical and serological findings. In a check examination in all cases. Considerable efforts were made to follow cases after treatment. In Series A at 3 months 60 and 66 per cent respectively were re-examined. Observations in all series are to continue for one year.

In Series A skin lesions began to dry in 24 hours pain in the joints and plantar and palmar yaws disappeared in 2-3 days. In most cases healing was complete in one month—a few ulcerated primary lesions with bacterial infections had healed by the second month. In Series B and C all lesions had healed in 3 months except three ulcerated primaries. [These were probably primary lesions in pre-existing ulcers in these the ulcers are unaffected by anti-yaws chemotherapy.]

At 6 months in Series A only two cases showed possible plantar lesions indicating relapse. At 3 months in Series B one case was similarly a possible relapse preceded these clinical manifestations. However no serological tests including the Quantitative Kahn and Quantitative Kolmer tests were employed and were carried out at the Army Medical School Washington.

At the end of 6 months only 17 cases (10 per cent.) in Series A had negative Kahn tests the others showed slight reductions in titre. Similar results were observed at 3 months in Series B and C in which only one case had a negative Kahn test.

Dark field examinations were negative in 8-12 hours after treatment a biopsy material was negative for spirochaetes after 22 hours.



TABLE 1  
Age distribution of and total amount of penicillin given to primary and secondary yaws patients

Age groups	5 years and under	6-12 years	13-18 years	17 years and over	Total	Vehicle	Method of administration
Series A— Total dosage penicillin in 4 days	13 1,200,000 O.U.	60 1,200,000 O.U.	41 1,200,000 O.U.	86 1,200,000 O.U.	200	Penicillin sodium in aqueous solution	Hospitalized. Intramuscular injections of 40,000 O.U. every 3 hours
Series B— Total dosage penicillin in 2 days	0	74 600,000 O.U.	27 900,000 O.U.	50 1,200,000 O.U.	151	Penicillin calcium in peanut oil with 4.8 per cent benzocaine by weight	Intra muscular injections at intervals of 24 hours
Series C— Total dosage penicillin in 1 day	0	58 600,000 O.U.	35 900,000 O.U.	58 1,200,000 O.U.	149	Same as Series B	Intra muscular injections at an interval of 10-12 hours
Total number patients	13	100	103	184	500		

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No severe toxic reactions were encountered. Half the patients in Series A had a pyrexia (100-104°F) 2-8 hours after treatment started. These had subsided in 10-12 hours. One-fifth of the patients had secondary pyrexia on the 3rd-5th days of treatment.

The authors point out that in active early syphilis similar prompt clinical response would have followed the same treatment but after 6 months 70-80 per cent (some British figures are higher) would have had negative serological tests. It is unlikely that concomitant malaria or syphilis interfered with the serological tests. From the results in Series A in which children and adults received equal doses it would appear that doses in excess of an optimum have no proportionate curative effect. The results of observations for months will be reported later.

C J Hackett

STUBENBORD W D Yaws  
Aug 1 39 No 8 603-9 2 figs

A report of a single case

Treatment with Penicillin. *Southern Med J* 18

## HELMINTHIASIS

HERNÁNDEZ MORALES F OLIVER-GONZÁLEZ J & PRATT Caroline K The  
Treatment of Schistosomiasis Mansonii with Urea Stibamine (Squibb)  
Preliminary Report *Amer J Trop Med* 1946 May 1 26 No 3 327-9

Encouraged by the results of treating human filariasis with pentavalent antimony compounds in intensive doses [CULBERTSON, ROSE and OLIVER-GONZÁLEZ this *Bulletin* 1946 v 43 54 354] the authors have used urea stibamine (Squibb) in the treatment of 14 cases of schistosomiasis due to *S. mansoni*. The cases chosen were those only who were passing large numbers of live schistosome ova. The patients consisted of seven male and seven female Porto Ricans aged from 12 to 36 years averaging 26 years for men and 21 for women. Accurate clinical records were kept. Only one-third of the patients showed symptoms referable to schistosomiasis.

Three daily intravenous doses were given after a small initial dose of 50 to 75 mgm. was given to detect susceptibility. Thereafter dosage was gradually increased to maximum tolerance.

The amount of the drug tolerated varied from 3.4 gm. to 10.125 gm. The smallest dose was given to a 12 year-old white girl of 73 pounds weight who never tolerated more than 150 mgm. the largest was received by a 29-year-old white male of 131 pounds weight. On an average the men tolerated 7.18 gm. throughout 16 days and the women 6.69 gm. throughout 13 days.

Toxic reactions were immediate or delayed. The former included flushing, facial oedema, hoarseness, dyspnoea, tachycardia, abdominal pain, nausea, vomiting, conjunctival congestion and a semi-shock-like condition. Delayed symptoms were generally milder. One death occurred on the 9th day of treatment in a woman who had received a total of 5.03 gm. of the drug.

Four patients showed traces of albumin and casts during treatment. At the end of treatment 10 patients still showed ova. After one, two, three and four months 12 patients had completely negative stools. The remaining patient, who only received 3.4 gm. of the drug, was still passing ova 60 days after treatment. The authors consider that the true evaluation of the drug can only be made after examinations through longer periods of time than the four months recorded but they find the results encouraging. H J O D Burke-Gaffney

ANDERSON J M. *Schistosomiasis and its Control in Egypt*. U.S. Nav. Med. Bull. 1946 July v 48, No. 7 977-1010 7 figs. [13 reb.]  
This is a general account of the subject, illustrated by admirable photographs.

AVERTY J L. The Habitat of the Snail Host of *Schistosoma japonicum* in the Philippines. *Science* 1946 July 5 5  
In 1932, TURANGUI see this Bulletin 1933 v 30 210 reported a fresh-water snail, at present designated as *Schistosomophora quadrasi* (Möllendorff) to be the intermediate host of the causative agent of schistosomiasis in the Philippine archipelago.

*S. quadrasi* has been reported from eastern Leyte eastern Mindoro northern Samar and around Palo Leyte in early 1945. The species is amphibious, but its preference for an aquatic environment is proportional to the temperature. The molluscs were often found as much as four inches above the water surface, on emergent vegetation but in the hotter parts of the day they migrated beneath the surface particularly in the shade of trees and shrubs. They were found principally in shallow quiet water containing much decayed organic matter particularly coconut fronds. The water usually showed a pH of about 8.0. There was often much pollution from human wastes and in one area 38 per cent of the *S. quadrasi* examined contained stages of human schistosomiasis. Five other species of molluscs were found in the same habitats.

H J O'D Burke-Gaffney

NELSON E C & BAYLIS M. *Schistosomiasis Japonica*—Laboratory Diagnosis. *Bull. U.S. Army Med. Dept.* 1946 v 5 No 6 673-80 5 figs.

The authors found that direct smear zinc sulphate flotation and acid-ether extraction techniques were not entirely suitable for diagnosis of eggs of *S. japonicum* mainly on account of the coated condition of the eggs, which was characteristic of the cases with which they worked. A sedimentation method was therefore devised which proved satisfactory and is designated the continuous floor funnel sedimentation technique.

Five to ten grammes of faeces are thoroughly mixed with 100 cc. of tap water and passed through a 20-mesh screen into the funnel assembly. This consists of a glass funnel with an overflow tube which fits tightly into the funnel outlet and whose upper extremity is a little below the rim of the funnel. Water is run rapidly into the funnel from above through a fine inlet tube with a bent tip which is placed at the outer edge and parallel to the side of the funnel at a level slightly below the top of the overflow. When the water is about to overflow the rate of flow is reduced to 100 cc. per 5 minutes. A slow whirlpool is created which carries off fine material through the overflow tube while the eggs settle at the bottom of the funnel. Ten minutes of this part of the technique is adequate. The overflow tube is then pulled out and the settled sediment released into a urine glass allowed to settle again and then examined. (It is to be regretted that the illustration of the apparatus cannot be reproduced satisfactorily in this Bulletin.)

J J C Buckley

FISHBOY H M. A Case in which Eggs of *Schistosoma japonicum* were demonstrated in Multiple Skin Lesions. *Amer. J. Trop. Med.* 1946 May v 28 No. 3 319-28 8 figs.

This case relates to a sergeant in the U.S. Army who was stationed on the island of Leyte in the Philippines for about a fortnight in November/December 1944. He had bathed in a slow running stream on the banks of which snails were found.

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About a week after his departure he noted angioneurotic swellings about both eyes which later involved the whole face. This lasted for three days and was accompanied by constitutional symptoms the fever which lasted for two weeks being followed by a dry nocturnal cough persisting for three weeks.

With the cough there developed grouped pruritic papules on the right subchondral wall together with a small evanescent group on the right side of the scrotum. The rash extended slowly towards the left abdominal wall axilla and back apparently in an intercostal-distribution. The lesions consisted of infiltrative groups of shotty papules.

Early in February examinations were otherwise without significance except a ray and laboratory examinations were found in the stool. Physical for an eosinophilia of 15 per cent.

The author gives a full description of the lesions which were not vesicular being herpetiform only in distribution and grouping which showed a predilection for the 8th intercostal space.

Biopsies of the abdominal wall and back lesions showed inflammatory reactions which included eosinophiles surrounding distorted schistosome ova. The latter were better preserved in the specimen from the back and the con- tained miracidia were well stained. Four photographs and two micro- photographs illustrate the lesions clearly.

Two courses of Fouadin were given each consisting of 40 cc. and lasting for a fortnight. The last new skin lesion containing ova with active miracidia was found ten days after completion of the first course. On the last observation of the patient two weeks after the second course the skin lesions appeared as small white fibrotic papules. The eosinophilia fell to 10 per cent. after the first course and to 9 per cent. after the second. Proctoscopy revealed no schistosome nodules but the stools remained positive for *S. japonicum* ova throughout.

The authors point out that whilst portal infiltrations by *S. japonicum* have been described and cases of cerebral and pulmonary involvement have been noted no adult worms of this species have been described in these vessels in man. The case under review manifests systemic involvement as well. Whilst the author considers the possibility of embolic skin lesions from a distant adult worm he also believes that such a worm may have been situated in an inter- costal vessel. He refers to the case reported by GARCIA *et al* [this Bulletin 1941 v 38 43] in which *S. japonicum* eggs were found in a skin biopsy from a child suffering from a chronic ulcer of the leg.

H J O D Burke-Gaffney

CARROLL D G Cerebral Involvement in Schistosomiasis japonica Bull  
Johns Hopkins Hosp 1946 Apr v 78 219 [Summary taken from  
J Amer Med Ass 1946 July 20 v 131 No 12 1023.]

Carroll reports five cases of cerebral involvement in schistosomiasis japonica which occurred among American officers and soldiers between the ages of 20 and 29 years on the island of Leyte in 1944. In all the cases ova of *Schistosoma japonicum* were found in the stools. There was a history of exposure and clinical symptoms and laboratory evidence suggestive of schistosomiasis japonica. Four of the patients presented neurologic involvement in the acute stage of the disease and one patient showed neurologic involvement four months after the acute stage. Those in the early stage had an acute onset of drowsiness followed by coma and incontinence. There were signs of pyramidal tract involvement with weakness spasticity and exaggerated deep reflexes. There was moderate eosinophilia. Symptoms improved with therapy. Neuro- logic involvement in the late stage was manifested by jacksonian convulsions.

followed by the development of hemiplegia but without drowsiness, coma or incontinence. The leukocyte count and eosinophil count were normal. There was no improvement with therapy.

CAMERON, T. W. M. **Fish-carried Parasites in Canada.** (1) Parasites carried by Fresh Water Fish. *Canadian J Comp Med* Gardenville Quebec. 1945 Sept Oct & Nov v 9 Nos 9 10 & 11 245-54 283-6 302-11 7 figs. [17 refs.]

This is a paper of much interest to veterinarians and to comparative pathologists written with Professor Cameron's known clarity and succinctness. It will appeal less to human pathologists and physicians because three only of the many species of helminthic parasites referred to infest man, and of one of these only a single case—and that rather doubtful—is on record.

Of the Heterophyidae several species are known to infest domestic cats, dogs, rabbits, white mice and a number of birds. In the Philippines, recently four different species were found in nine autopsies, and as four of the patients had died from cardiac trouble it was believed that there was some aetiological connexion between them.

The life-histories of *Anophallus renatus* and 4 *brans* are described in full and diagrammatically depicted. Each has two intermediate hosts in the case of 4 *renatus* the first is the small *Goniobasis incens* the cercariae from this attach themselves to the base of the fin of some fresh-water fish (13 are named among them carp, dace, perch and catfish) shed their tails and penetrate the infested fish is eaten by a mammalian or avian host. In the stools of a man in Ste. Anne's Military Hospital, Canada were found helminth ova agreeing in appearance with this species.

Another trematode infesting man and also the dog, red fox, mink, raccoon and cat but not birds, is *Uvicorchi*. The life-histories of some species of this genus are unknown but that of *M. conjunctus* is fully described. It is closely similar to that of *Opisthorchis* and *Clonorchis* with two intermediate hosts the small *Ammocete* and a fish, the common sucker (*Catostomus commersoni*). Only in places where the sucker is eaten raw does man become infested.

*Clinostomum marginatum* occasionally infests man. [Another species has been recorded in man in Japan and is the cause of parasitic laryngopharyngitis known as *Halzoun* in the Near East. See this Bulletin 1945 v 42, 306.] The small intermediate host is *Helicostomus tricolor macrostomus* "but other related Planorbis-like snails may also serve as vectors." Its cercaria has a forked tail and encysts on fins or gills or beneath the scales of certain fish, and produces small abscess-like cysts so that man rarely eats it.

Lastly there is a *Dipyllobothrium* closely related to the European *D. latum*. Its first intermediate hosts are fresh water crustaceans, *Diplomona oregonensis*, *D. sicilis* and *D. siciloides* and the plerocercoids are found in pike and perch. It is one of the commonest cestodes in man in eastern Canada and is found also in dogs often and in foxes, cats and bears less often. Other tapeworms with fish as intermediate hosts which may be mentioned, are *Lagus trinaeophorus* and *Proteocephalus* but these are not infective for man or for domestic animals.

H. Harold Scott.

JONES, J. M. & RE, P. M. *Hydatidosis y procesos graves anaflácticos* [Hydatid Disease and Severe Anaphylaxis]. *Rev. Asoc. Med. Argentina*. 1948 June 15, v 60 No 583 445-50 [21 refs.]

PULLAR, E. M. **A Survey of Victorian Canine and Vulpine Parasites. III. Platyhelminthes other than Taenia.**

In this short paper the author discusses some of the still vexed questions of hookworm disease. He points out that the African with hookworm is usually suffering from other parasitic diseases also—malaria schistosomiasis—or from malnutrition or disorders of the liver and that too exclusive a concentration on the diagnosis of hookworm disease on the evidence of ova in the stool, may be disastrous to a patient. The injudicious administration of an anthelmintic may be fatal in a patient seriously ill from another cause. In dimerphic anaemia (which is the common anaemia of Africa) a cause for the iron loss such as hookworm schistosomiasis malaria or dysentery can usually be demonstrated and it is unlikely that the intake of iron in Africa is unduly low though the nutritional factor in anaemia is extremely important. Treatment for hookworm infestation alone is therefore usually insufficient to cure anaemia and, in fact this mixed anaemia is difficult to treat successfully. In the European the matter is usually very different anaemia is slight or absent but abdominal pain and flatulence are common.

The author has not found that increase in appetite is a marked symptom of hookworm disease although so often mentioned in text-books nor is earth-eating peculiar to those with hookworm in spite of common opinion. Earth-eating is practised by many African tribes partly as a result of the belief that it increases fertility partly as a ceremonial but since many of the earths are rich in salts of iron calcium magnesium and sodium there may be a physiological basis for earth-eating.

The author believes that there is some degree of toxæmia in hookworm disease which, in a few cases may be responsible for fever eosinophilia and oedema when these cannot otherwise be explained. Charles W. Ilcocks

ROGERS A M & DAJOU G J Hookworm Infection in American Troops in Assam and Burma. Amer J Med Sci 1946 May v 211 No 5 531-8

Differing from the traditional picture of hookworm disease the prominent features in 50 consecutive cases in combat troops in North Burma were gastrointestinal symptoms of abrupt onset and lack of anaemia. There were nausea and vomiting with abdominal pain, usually epigastric arising immediately after meals and not relieved by food. Diarrhoea was a prominent sign but blood pus and mucus were not found in the stools. By questioning a history of ground itch was obtained from a quarter of the patients and a history of respiratory symptoms from 70 per cent. but the value of these histories is doubtful. All the patients had lost some weight ranging from 10 to 40 lb but loss of weight was common among all combat troops in Burma. Some patients had a low-grade fever and a few had attacks of urticaria. A striking feature of the infection was the degree of eosinophilia, the discovery of which first led in many instances to the examination of the stools. The maximum eosinophilia was 70 per cent with a total leucocyte count of 41 000 per cmm. but the more usual finding was eosinophilia of 40 per cent. with a total count of about 15 000 leucocytes. The earliest time for appearance of eosinophilia after the suspected date of infection was 30 days and the eosinophilia persisted to a diminished degree for weeks and months despite frequent vermifuge treatment. Anaemia was neither marked nor constant. Direct examination of the stool revealed initially only 20 per cent of the infections but by repeated direct examinations it was possible to establish the diagnosis in a little more than half the patients. The zinc sulphate flotation-centrifugation method increased the number of positive findings four fold, and

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proved a rapid and efficient means of finding eggs in the stool in all cases the diagnosis was confirmed by the finding of eggs by one or other of these methods. The routine treatment consisted of 3 cc. of tetrachlorethylene, given in the morning after a fat free supper followed by a magnesium sulphate purge on the previous evening. A second purge was given 2 hours after the vermifuge. If treatment failed, it was repeated after an interval of 3 weeks. Sometimes carbon tetrachloride or hexyresorcinol was used. One week or more after treatment the stools were re-examined. 20 per cent of the patients still showed eggs although on the average they had been treated twice.

The anorexia, vomiting and diarrhoea were most readily relieved by treatment while the cramping pain after meals was the slowest symptom to disappear and the one which persisted in those who were unimproved. It should be pointed out that not all the patients showed the acute syndrome described and in fact many asymptomatic infections were discovered by the routine examination of the stools of patients admitted to hospital for some other condition.

F Murgatroyd

STUBENBORD W & ALLEN R F Hookworm Disease in Infants. Report of Two Fatal Cases. *U.S. Nav Med Bull* 1948 June v 46 No 6 915-17

Hookworm disease is rare in infants under one year of age partly because they do not often come into contact with infected soil. The author records two cases from Guam in which massive infection was present in such infants. In the first infant moribund on arrival at hospital 300-400 adult *Angiostrongylus duodenalis* were present in the intestine the child was anemic and there was fluid in the pleural and abdominal cavities. In the second (dead on arrival at hospital) there were several hundreds of *A. duodenalis* many haemorrhagic areas in the mucosa of the small intestine, and extreme anaemia.

Charles Willocks

SCOTT J A Simplified Quantitative Methods for Hookworm Control Programs. *Amer J Trop Med* 1948 May v 28 No 3 331-7 1 fig

The final answer to the problem of the control of hookworm disease is improvement in environmental sanitation. In Georgia, sanitation programmes have not yet reached the families most affected and are unlikely to do so for many years. Interim measures are therefore necessary.

The public health authorities have aimed at treating the most heavily infected members of the community with the objects of obtaining the maximum reduction in the source of infection and of relieving the symptoms in those most affected.

It is now generally agreed that the pathogenicity of hookworms is fundamentally based on their blood letting activities that anaemia is the primary symptom and that all other manifestations are secondary to it. The extent to which the severity of anaemia is related to the intensity of hookworm infection is often obscured however by a nutritional factor. Apparently most well nourished persons have enough immunity to prevent the most heavily infected members of the community with the objects of obtaining the maximum reduction in the source of infection and of relieving the symptoms in those most affected.

In certain states of malnutrition this protective mechanism is weakened and large numbers of worms become sufficient to cause appreciable anaemia. In certain states of malnutrition this protective mechanism is weakened and large numbers of worms become sufficient to cause appreciable anaemia. Imbalance may of itself cause anaemia. Hookworm disease is then primarily the result of the additional drain which the worms place upon a hemopoietic system already nearing if not past its maximum limit of compensatory reaction. In evaluating the seriousness of hookworm disease there are two factors to be considered. The first is a determination of the degree of anaemia

which can be accurately done by the use of a hemoglobinometer or approximately estimated from the clinical signs. The second is a necessity for determining what portion of the anemic condition is due to the basic state of malnutrition and what portion to the superimposed hookworm infection. HILL and ANDREWS in this *Bulletin* 1943 v 40 324] showed that in Georgia no measurable depression of the average hemoglobin reading was associated with hookworm egg counts of less than 2,500 per cc [the figure corrected for the consistency of the stools was 5 000 per cc]. Above this point however a progressive drop in the hemoglobin reading was correlated with the size of the egg count. From these data it was concluded that in Georgia all of the cases of hookworm disease would be found in the group whose counts were above 2 500 eggs per cc. In practice the order of making these determinations is reversed.

In annual examinations of the schoolchildren the clinically grossly anaemic are selected. The border line cases are checked by haemoglobin examination. egg counts are made on all anaemic children. The families of children with more than 2,500 eggs per cc of stool are visited and those found infected are treated.

There are limitations to the accuracy of this method of selection and further it involved the use of statistical methods which are not simple enough for general application in a health programme. In this paper a modification of this procedure is described.

The data are based on the examination of specimens collected from rural, white families by a visiting nurse. These families were chosen at random from over the whole country except for the fact that obviously well-to-do families were not included. Specimens were examined by a salt flotation method and the positives were re-examined by egg count using the technique as modified by Stoll and Hausheer.

After some necessary adjustments have been made owing to the fact that it was not possible to do egg counts in every case in which the flotation method showed eggs the data are arranged as in the example given below. [While the adjustments that were made would satisfy most statisticians it seems that they could have been obviated by the collection of larger samples of stool in every case.]

Hookworm infection in Brantley County Georgia in 1942				
Age Group	No of persons examined	Percent. infected with hookworm*	Percent. positive by egg count†	Percent. of suspected cases of hookworm disease ‡
0-4	160	49.4	45.6	23.4
5-19	514	67.7	63.8	32.6
20+	150	46.7	38.2	11.3

\* Per cent. positive by flotation. † With 200 or more eggs per cc.  
‡ With 2,500 or more eggs per cc.

This table gives all the important data for the practical use of the health officer but for the use of the statistician for comparison with data in which different levels of significance have been used, further calculations have to be made. The author shows how a normal curve based on the figures of the fourth and fifth columns of the table approximate very closely the normal curve based on the entire series of egg counts and he therefore considers that these two figures will supply sufficient data for most statistical purposes.

L. E. Napier



- I. ROCHA E SILVA, M & GRAÇA R. Anaphylaxis-like Reactions produced by *Ascaris* Extracts. I. The Change in Histamine Content and the Coagulability of the Blood in Guinea Pigs and in Dogs. *Arch Surgery* 1946 May v 52 No 5 523-37 4 charts. [Refs. in footnotes.]
- II. — & — II. The Mechanism of the Shock Induced in Dogs. *Ibid* 1946 June v 52 No 6 713-28 6 charts. [Refs. in footnotes.]
- III. — PORTO A & AMBRADE Sylvia O III. The Role played by Leucocytes and Platelets in the Genesis of the Shock. *Ibid.* Aug. v 53 No 2 199-213 3 figs. [20 refs.]

I. In an earlier paper (to be published) the authors studied the mechanism of shock produced by hydatid fluid injected into dogs and concluded that the substance which caused the shock is not precipitated by 5 per cent. trichloroacetic acid, does not dialyze through Cellophane paper and resists boiling for a long time. They obtained a fairly well-purified material which produces profound shock in dogs the shock being indirect, because a second injection produces no appreciable effect (desensitization). In some instances they also found an evanescent incoagulability of the blood (complete incoagulability in some animals) which suggested the liberation of heparin from the tissues into the blood. They found that histamine in the circulating blood of a few animals was increased, but that in most of the animals the histamine in the blood was decreased, although GRAÇA *et al.* found that histamine was increased in every dog into which hydatid fluid was injected. The authors decided to find out whether nematodes may contain substances which produce shock.

LEROY (*Arch. Internat. de Physiol.* 1910 v 9 276) and EMERY and HERRICK (*Amer. J. Physiol.* 1929 v 91 143) found that extracts of *Ascaris lumbricoides* produce hypotension in dogs. SHIMAMURA and FUJI (*J. Coll. Agric.* 1917 v 4 186) quoted by ESSEX, MARKOWITZ and MANN (*Amer. J. Physiol.* 1931 v 98 18) isolated an albumose peptone which was very toxic to dogs and called this substance askeron. MACHEBOEUR and MANDOUZ (*C. R. Soc. Biol.* 1939 v 130 1032) produced in guinea-pigs with extracts of *A. lumbricoides* emphysema not distinguishable from that produced by anaphylactic shock. The material which did this was soluble in 4 per cent. trichloroacetic acid and in 50 per cent. ethyl alcohol and it was not removed by dialysis. BIER (personal communication to the authors) showed in 1939 that a substance in *A. lumbricoides* produces shock resembling anaphylactic shock in guinea-pigs. The present authors observed that extracts of *A. lumbricoides* produce severe or fatal shock in dogs which has features of anaphylactic shock, namely liver congestion incoagulability of the blood, desensitization after recovery and the appearance of histamine in the blood. The shock is however very severe and nearly all the dogs react violently to a few cubic centimetres of the extract.

The material used for the experiments here described was obtained from *Ascaris lumbricoides* ground in a colloid mill, the pulp obtained being treated with an equal volume of 10 per cent. trichloroacetic acid for 2 hours at room temperature and then left overnight in the refrigerator. The opalescent fluid thus obtained was dialyzed through cellophane for at least 48 hours until it was freed from trichloroacetic acid. The pH was then adjusted to neutrality with sodium carbonate and the fluid was used. For details of the further purification of this material the paper itself must be consulted. The tests done suggested that the substance causing shock in dogs is not a protein but a proteose of large molecular weight. A glycogen fraction was also prepared, which was apparently related to the polysaccharide prepared from *A. lumbricoides* by CAMPBELL (*J. Infect. Dis.* 1936 v 59 266). Antithrombin assays

of the blood of the dogs were done with a solution of human prothrombin prepared by the method of QUICK (*Amer J Physiol* 1936 v 116 535)

For details of the experiments done and for the authors' comments upon them the paper itself must be consulted. The authors found that deproteinized and dialysed extracts of *A. lumbricoides* produce a severe form of shock in dogs accompanied by enormous engorgement of the liver, drastic reduction of the liver histamine, increased histamine in the blood, the appearance of an antithrombin (heparin) factor in the circulating blood, and desensitization. The main increase of blood histamine occurred in the portal vein six times higher than that in the femoral vein. Crude extracts of *A. lumbricoides* produced massive emphysema in guinea pigs and death in a few minutes. In a few guinea pigs increase of the blood histamine was observed.

The authors discuss the allergic nature of this anaphylaxis-like reaction. Most of the dogs used had heavy infections with intestinal hookworms; injection of *Ascaris* extracts produced skin reactions so that it is possible that most of the dogs in Brazil are sensitized by intestinal nematodes and that thus sensitization is allergic rather than anaphylactic. The authors emphasize their view that a distinction cannot be drawn between allergy and experimental anaphylaxis.

ii In their second paper the authors record experiments which follow up the work recorded in their first paper which showed that injection of *Ascaris* extracts into the veins of normal dogs causes a discharge of histamine into the general blood circulation. Because there is considerable decrease of the total histamine which can be extracted from pieces of liver taken after the shock produced by the *Ascaris* extracts has occurred, the authors conclude that most of the histamine discharged into the blood during the shock comes from the liver. In this second paper experiments are, however, recorded which show that the *Ascaris* extracts cannot cause a discharge of histamine from the livers of dogs previously sensitized by two subcutaneous injections of the *Ascaris* material when these livers were perfused with Tyrode solution or defibrinated blood. Two of the dogs used for these experiments had been previously sensitized to horse serum but the perfusion of horse serum through their livers did not cause a discharge of histamine. The authors therefore concluded that direct contact of the antigen with the sensitized liver cells is not enough to cause discharge of histamine. In identical circumstances trypsin and mercury bichloride perfused through the livers regularly caused a discharge of copious amounts of histamine.

The authors also describe in this paper a mechanical type of shock observed in about 5 per cent of the dogs into which *Ascaris* extracts were injected. This form of shock is characterized by a profound fall in the blood pressure in the carotid artery but no increase of the blood histamine or heparin. Apparently it depends upon a mechanical obstruction of the hepatic blood vessels by clumped leucocytes and blood platelets without very much discharge of active substances.

Experiments are also described which indicate that the intravenous administration of liver glycogen partially or completely desensitizes the animal to the *Ascaris* extract and that the discharge of histamine and heparin from the liver cells can be entirely prevented by the administration of glycogen. The authors adduce as the explanation of this inhibition the fact that liver glycogen almost entirely removes platelets from circulating blood and causes severe leucopenia.

iii The authors of this paper follow up the conclusion of ROCHA E SILVA and GRAÇA (see ii above) that the contact of *Ascaris* antigen alone with

the cells of the liver of the dog is not enough to produce an appreciable discharge of histamine from the liver cells. They claim that they have shown that the blood contains all the constituents which are necessary to do this when *Ascaris* antigen is added to the system.

The preparation of the *Ascaris* extracts and the method of perfusing the liver were those which were described in the earlier papers except that the blood (800 cc.) used for perfusion was collected over a 3.8 per cent solution of sodium citrate (200 cc.) in a paraffined beaker. For the methods of estimating the velocity of the perfusion, the number of the blood platelets and the amounts of histamine, heparin and plasma trypsin the paper itself must be consulted.

The authors conclude from all their results that the shock produced by *Ascaris* extracts and anaphylactic shock have the same mechanism. When the isolated liver of the dog is perfused with citrated whole blood contained in paraffined receptacles a conspicuous decrease of the leucocytes and blood platelets follows the injection of *Ascaris* extracts into the cannula. Usually small amounts of histamine and of an anticoagulant (heparin) are released into the perfusing blood and in one instance considerable amounts of both were discharged from the perfused liver. This definitely shows that intact blood contains the factors which are necessary to produce a release of histamine and heparin from liver cells when the [*Ascaris*] extract is added.

Microscopical examination of smears made from pieces of liver taken before and after the shock in the intact unanaesthetized dog showed that platelets formed enormous aggregates which disappeared or partially disintegrated during the later stages of the shock. Plasma trypsin free and total, was estimated in the blood used for perfusion before and after injection of the *Ascaris* extracts. Similar estimations were made in the circulating blood of the intact dog which was given *Ascaris* extracts intravenously. Although, in a few instances there was a clear indication of the activation of plasma trypsin, usually there occurred, especially at the height of the shock, a definite decrease of free trypsin. This decrease of free trypsin was attributed to the appearance of heparin in the circulating blood. The authors discuss the probable chain of reactions which leads to the discharge of histamine and heparin from the parenchyma of the liver of the dog during anaphylactic shock and give a diagram of these. They also discuss the correlation between these reactions and the clumping and disintegration of blood elements especially the platelets which occur in the liver capillaries.

G. Lapege

CLIMO G. R. COCKER, W. & HORNBY S. The Constitution of Santonin. Part IV  
*J. Chem. Soc.* 1946 July 616-17

WHARTON D. R. A. & STELMA, T. Comparative Cutaneous Tests for Filariasis with Antigens of Different Dilutions. *J. Infect. Dis.* 1946 Jan.-Feb. 178  
No. 1 49-59 11 refs.]

It is not possible to summarize here the interesting details contained in this paper. The publication and discussion of them are valuable because they illustrate important sources of error against which those who attempt cutaneous tests with filarial antigens have to guard. This abstract may advantageously be read together with that of WARREN *et al.* printed below.

The authors of the present paper summarize some of the relevant literature and point out that the cutaneous test for filariasis has two weaknesses—it cannot differentiate between infections with the different species of filaroid nematodes parasitic in man, and some 10 per cent. of the tests done give false

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positives (see however below) The antigen used was prepared from vacuum dried specimens of *Dirofilaria immitis* ground up with saline to make a dilution of 1:100. This dilution was then frozen and thawed alternately twice during one day, heated for four hours at 56°C and centrifuged at 2,500 r.p.m. for 30 minutes. The supernatant extract was then fractionally sterilized with physiological saline for use. The authors think that the general opinion is that the immediate reaction is the significant one and that the index of the strength of the reaction is in the following order: erythema, weal, a weal with pseudopodia, singly or in combination. The present authors made their injections on the flexor surface of the forearm at a distance of 10 cm apart but even when this was done the swelling and erythema of delayed reactions sometimes became confluent with the areas into which weaker dilutions of antigen and the control fluid were injected. The control fluid was dog serum fractionally sterilized at a dilution of 1:100 preserved with 0.3 per cent phenol and used at the same dilutions as those of the filarial antigen. Delayed reactions resulted when the stronger antigens were used. These could begin as early as one hour after the injection but did not develop in one case until three days after it. In some cases the arm was incapacitated by the delayed reaction. The delayed reaction in filariasis usually develops rapidly and is a deep extensive swollen erythematous rubbery zone which itches and feels heavy. Fairley identifies it with Calabar swelling.

Four series of subjects from the Dutch West Indies together with 4 other members filarous seamen from the same endemic area. These men were tested with antigen dilutions of 1:1,000 and 1:8,000. Series 1 were 29 of the same ship's crew from the same endemic area and most of whom were series 1 and consisted of 54 non-filarious individuals from a history of filariasis of the New York Hospital all of them being allergic to various substances. Series 3 was composed of 153 individuals from a history of filariasis and most of whom were exposed to infection in an endemic area and most of whom were exposed to infection in an endemic area. These men were tested with antigen dilutions of 1:1,000 and 1:8,000. Series 2 acted as controls or had been exposed to infection in an endemic area. These men were tested with antigen dilutions of 1:1,000 and 1:8,000. Series 4 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 5 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 6 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 7 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 8 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 9 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 10 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 11 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 12 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 13 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 14 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 15 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 16 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 17 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 18 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 19 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 20 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 21 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 22 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 23 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 24 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 25 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 26 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 27 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 28 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 29 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 30 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 31 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 32 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 33 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 34 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 35 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 36 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 37 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 38 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 39 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 40 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 41 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 42 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of 1:1,000 to 1:100,000 of the antigen and 1:20,000 of the dog serum control fluid used to test this series was diluted to 1:100,000. Series 43 consisted of 46 men under observation for filariasis or other infections acquired in the South Pacific. These were tested with dilutions of

species *Litomosoides carinii* tolerated massive doses of *Dirofilaria immitis* material (up to 25 mgm. of powdered *Dirofilaria immitis* in physiological saline). When death of these rats was caused by higher doses it appeared to be due to anaphylactic shock. G. Lafage

WARREN Virginia G. WARREN J & HUNTER, G. W. Studies on Filariasis. I. Serological Relationships between Antigenic Extracts of *Wuchereria bancrofti* and *Dirofilaria immitis*. *Amer J Hyg* 1946 Mar \ 43 No 2, 164-70 1 fig 12 refs

The authors set out to seek for the diagnosis of filariasis a better test than biopsy or the discovery of microfilariae in the blood. They summarize the contents of several papers, all of which have been abstracted in previous issues of this *Bulletin* which record results obtained with antigens obtained from the filaroid species *Dirofilaria immitis*, *Litomosoides carinii* and *Confortospiculus rileyi*. The authors say that it is generally agreed that extracts of these species will give cutaneous reactions in persons infected with *Wuchereria bancrofti* and that precipitin and complement fixation tests done with them are also successful to a certain degree. Antigens have also been made from *Wuchereria bancrofti* see ACTON and RAO this *Bulletin* 1933 v 30 699] and OLIVER-GONZÁLEZ and BERLOVITZ [this *Bulletin* 1945 v 42 219], but these gave disappointing results.

The present authors made antigens from the microfilariae of *W. bancrofti* and also from adult *D. immitis*. They describe in detail the methods used for making them. Microfilariae of *W. bancrofti* were isolated from human blood by centrifugation, frozen, dried *in vacuo*, powdered, dried again over  $\text{CaCl}_2$  and a 1 per cent suspension was then made in physiological saline. This was refrigerated at 5°C. for 24 hours and then alternately frozen and thawed several times and put in a water bath at 56°C. for 4 hours and often shaken to decrease any anticomplementary properties. It was then centrifuged at 500 r.p.m. for 10 minutes. The process was sterile throughout. The resulting supernatant fluid was used as the antigen being preserved by the addition of 0.3 per cent phenol. The sediment was used for the immunization of rabbits. The control used was a leucocyte-stroma antigen made in the same way from normal human blood known to be free from microfilarial larvae. The *Dirofilaria immitis* antigen was made from dried adult specimens obtained from the heart and lungs of dogs. With these antigens the authors did complement-fixation tests, intradermal tests and studies of cross antigenicity. For the details of the technique of these experiments the paper itself must be consulted.

Complement fixation tests were done upon the sera of 12 subjects who had been clinically diagnosed as suffering from filariasis. Antigen dilutions of 1/100 and 1/800 were used with serum dilutions of 1/1 and 1/128. All the sera gave negative results with the *W. bancrofti* antigen even though motile microfilarial larvae were present in two of these sera. All the sera on the other hand, gave strongly positive fixation with the *D. immitis* antigen. The former antigen thus appears to be unsuitable for complement fixation tests. The authors thought that the failure of the *W. bancrofti* antigen might have been due to the use of an antigen deficient in a water-soluble component lost in the washings of the citrated blood used but all attempts to make an antigen containing this water-soluble component or to make a polysaccharide antigen failed to produce an antigen which would give positive results.

Intradermal tests were done on 32 soldiers who had recently returned from a hyperendemic area in the Southwest Pacific. They showed good clinical evidence that they were suffering from filariasis. The sera of 30 of these men gave positive fixation with *D. immitis* antigen, but microfilarial larvae

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were not found in the blood. Each man was given an injection of 0.025 ml of dilutions of 1 4 000 1 8 000 and 1 12 000 of the *W bancrofti* antigen and dilutions of 1 8 000 of the *D immitis* antigen. Control tests were done with 1 4 000 dilutions of the leucocytestroma antigen and with 1 8 000 dilutions of dog serum in physiological saline to which 0.3 per cent phenol had been added. The criterion of a positive reaction was a weal which had at the end of 10 minutes a diameter at least 3 mm greater than that of the control.

Of the 32 subjects 22 gave positive reactions to the *W bancrofti* antigen 23 were positive to the *D immitis* antigen 17 were positive to both and 4 to neither. Two subjects whose sera gave no complement fixation to *W bancrofti* antigen and yet contained microfilarial larvae gave positive intradermal reaction to *W bancrofti* antigen and strongly positive ones to *D immitis* antigen.

When 75 control subjects with a history of allergy were tested none of whom had been in an endemic area only four of them gave a cutaneous response to *W bancrofti* antigen. When 21 others infected with intestinal nematodes the species of which are not given were tested none gave a positive intradermal reaction with *W bancrofti* antigen.

In order to explain the discrepant results obtained with these two antigens the authors tried to prepare specific antisera. Four rabbits were immunized with 1 100 dilutions of both antigens and with sediments of worm material obtained from the centrifugation during the preparation of the antigens. Two rabbits were given the *W bancrofti* sediment and two were given the *D immitis* sediment all having 10 injections intraperitoneally. The sera of these rabbits were then titrated against the antigens and against the human leucocytestroma antigen for complement fixation. With both antigens a high titre occurred but the antisera also reacted to an equal degree with the leucocytestroma antigen. No fixation occurred however when normal rabbit sera were used.

To study cross-antigenicity one portion of a high titre *W bancrofti* serum was absorbed for 18 hours at 5°C with an excess of *W bancrofti* antigen a second portion with an excess of *D immitis* antigen and a third with the leucocyte-stroma antigen. Similar absorptions of a high titre *D immitis* antigen were done but none with the leucocyte-stroma antigen. It was found that absorption of antisera with the homologous antigen removes all activity from the immune sera but that absorption with the heterologous antigen removes only the heterologous antibody. The authors concluded that both the filarial species used contain a species specific and also a group-specific antigen.

G Lapage.

SUTLIFF W D & ANTONIO ECHANDI G R. Pinworm (*E. vermicularis*) and other Intestinal Parasites in Costa Rican Children. *J Parasitology* 1946 June v 32 No 3 233-6 [11 refs.]

DORIN R P. The Preparation and Demonstration of an Antiserum for *Trichinella spiralis*. *J Parasitology* 1946 Feb v 32 No 1 83-8.

The author describes the fixation of *Trichinella spiralis* antigen on to aluminum cream preparations by the method originally described by HERTOGH and WELKER (*J Infect Dis* 1933 v 53 308) and used successfully in the field of organ sera by SPRINKA and WEIGSELBAUM (*Proc. Soc. Exper Biol. & Med* 1938 v 38 447). MANN and WELKER (*Amer J Cancer* 1940 v 39 360) and COHEN and FREDA (*Proc Soc Exper Biol & Med* 1940 v 43 22). The author claims that the method makes possible a single injection of

the antigen and the use of material which need not be sterile and that the rabbit into which it is injected produces antibodies for a long while.

The author used larvae of *Trichinella spiralis* isolated from rat muscle by digestion, and washed in physiological saline until the Burret test was negative. If, he says this washing is not done the experimental animal dies possibly from peptone shock. The larval material was then absorbed on to aluminum cream by the method of WELKER and TRACY (*J. Biol. Chem.* 1915 v. 22, 55). The material thus obtained was then injected into rabbits by the method of Hektoen and Welker. Variations in the method of making the antigen resulted in the production of different titres in the antisera obtained, and these are discussed by the author. The antigen used to find the titre of the antisera was a commercial preparation made by the Eli Lilly Co. and used for intradermal tests in the diagnosis of trichiniasis. This antigen was adjusted to neutrality with acetic acid and its nitrogen content was determined by the Koch-McNeekum micro-Kjeldahl method. The author found that this antigen did not give a positive reaction with an antiserum made from rat tissue by the method of Spinka and Weichselbaum. None of the rat tissue antisera reacted positively with rat tissue autolysates made by the method of Mann and Welker. The antisera were usually made by the method of Spinka and Weichselbaum. It was found that the injection of a suspension of 400 000 *Trichinella* larvae in 80 cc. of saline with the addition of 120 cc. of aluminum cream gave after centrifugation the desired amount of material for injection into each rabbit. Each rabbit thus received 400 000 *Trichinella* larvae.

Injection of these antigens gave antisera with titres of 1 4 000 1 5 000 1 6 000 and 1 11 000. When rabbits were given by the mouth doses of larvae near the lethal dose antisera were obtained with titres ranging up to 1 8 000 according to the length of time since the injection.

The effect of the injection of these antigens upon the resistance of rabbits to infection with *Trichinella spiralis* was striking. Three rabbits were injected with antigen fixed on aluminum cream, and these were used as actively immunized animals. These and also five normal rabbits as controls were each given by the mouth 20 000 *Trichinella* larvae in 10 cc. of saline. Two of the controls died and one of the immunized rabbits died on the 32nd day from the effects of a bite by one of its mates. The others were killed on the 43rd day after the doses of larvae and equal weights of their muscles (tongue masseters diaphragms and muscles of the two forelegs) were digested. In one immunized rabbit the only larvae found were the ten in the muscles of one of the forelegs. The titre of the antiserum of this rabbit was 1 6,000. In the other immunized rabbit 90 larvae were found in the tongue 120 in the masseters, 150 in the diaphragm 200 in the muscles of one foreleg and 800 in those of the other. The titre of the antiserum of this rabbit was 1 5 000. In the controls from 7,800 to 12 000 larvae were found in the tongue from 16,900 to 23 700 in the masseters from 16 400 to 32,700 in the diaphragms, from 30,500 to 45 000 in the muscles of one of the forelegs and from 30 700 to 47,500 in those of the other. The conclusion was drawn that the actively immunized rabbits had resisted the infection.

It was found that injection of the immune sera also protected the rabbits. Six rabbits were given a sublethal dose of 4,500 *Trichinella* larvae. Three of them were then given 9 cc. of immune serum intraperitoneally in doses of 3 cc. each, one on the day before the larvae were given one on the day on which they were given and one on the day after they were given. The three other rabbits were given normal rabbit serum in the same way. Two uninfected rabbits were given the same amount of normal serum as an additional control. Eleven days later it was found that (a) the rabbits given larvae and immune serum were sleek active responsive and clean-looking and apparently normal.

## Deficiency Diseases.

(b) the rabbits given larvae and normal serum had bloody red noses and ruffled fur and were unresponsive and apparently moribund (c) the controls given normal serum only were normal The conclusion was drawn that the immune serum had protected the rabbits The author claims that the anti sera are specific to larvae of *Trichinella spiralis* but not for any of the blood proteins G Lafage

LEON L. A. Cuarto caso de infección humana por *Agamomermis*. [Fourth Case of Human Infection with *Agamomermis*] *Rev Med Trop y Parasit Habana* 1946 Jan-Mar v 12 No 1 25-6 3 figs

This paper describes a nematode found in the excreta of a mestizo child aged five who came for treatment for infection with *Ascaris lumbricoides*. The nematode is briefly described and the author regards it as a species of *Agamomermis* a name given to immature forms of species belonging to the nematode family Mermithidae which have been found in the past three times in human beings and are noted in text books of parasitology All are regarded as accidental parasites and the specimen here described is regarded by the author as an accidental parasite ingested with the food possibly with raw fruit [The Mermithidae are nematodes whose larval phases are parasitic in earwigs grasshoppers and some other insects the adult phases being non-parasitic and living in the soil *Agamomermis* should not be confused with *Agamermis* which is the name of a true genus of the family Mermithidae] G Lafage.

## DEFICIENCY DISEASES

CLARKE C A & SNEDDON I B Nutritional Neuropathy in Prisoners-of-War and Internees from Hong Kong *Lancet* 1946 May 18 734-7 [Summary appears also in *Bulletin of Hygiene*]

This report deals with the condition after their arrival in Australia of 200 patients who had been prisoners in Hong Kong from late 1941 until September 1945 On admission to hospital none of the patients showed any of the classical signs of vitamin deficiency but 74 of them showed grossly abnormal neurological signs which were classified as optic atrophy and ataxic paraplegia in 31 patients ataxic paraplegia alone in 21 optic atrophy alone in 13 optic atrophy nerve deafness and ataxic paraplegia in 6 and optic atrophy and nerve deafness in 3

The commonest neurological abnormality was impairment of visual acuity (53 cases) due to central and paracentral scotomata the ocular fundi showed partial optic atrophy and in many cases macular degeneration was present The parasthesiae sensory loss of stocking distribution ataxia foot-drop and loss of deep reflexes were like those of polyneuritis but tenderness of the calves was not found Some cases showed increased deep reflexes spasticity and ataxia out of proportion to the degree of anaesthesia and the condition of some suggested amyotrophic lateral sclerosis. No significant changes were found in the blood nor was there any evident relationship between neurological disturbance and achlohydria. No general lowering of the level of the plasma proteins was found and oedema was never a prominent feature.

Treatment for two months with a high-calorie diet and massive doses of vitamins led to subjective improvements in many cases but the neurological signs remained unchanged. The authors believe that the neuropathy they describe results from a toxic or antivitamin principle in the diet rather than from a plain dietary deficiency H E Harding



Scattered inflammatory cells as well as occasional small foci are still present in the upper layers of the corium. Some restitution has occurred in the basal layer and some of the rete pegs are of usual width and appearance. Others however show persistent degenerative changes in the basal layer with consequent sharpening of their outlines. Small masses of pigment are occasionally seen in the papillary and subpapillary connective tissue. When seen in this stage it is extremely difficult to differentiate this condition from other toxic dermatoses in tissue sections.

Certain histological changes are common to the three stages—these include thickening of the horny layer, blocking of the follicular orifices by keratin plugs and degenerative and liquefactive changes in the cells of the basal layer of the epidermis. Spongiosis often occurs. Usually there is an increase of pigment in the basal layer. A cellular infiltrate which varies with the severity of the disease and which chiefly consists of lymphocytes and histiocytes is present in the papillary and subpapillary layers of the corium, and tends to cluster round hair shafts, hair follicles and glandular tissues. Also aggregations of pigment can be noted—particularly in acute cases—in the two upper layers of the corium and most characteristically at the tips of the papillae. The pigment is a melanin and most of it is enclosed in macrophages although some may be scattered in the stroma.

Rosenthal gives full reports concerning blood examinations which were made in 18 cases. A moderate anaemia was found in 12 of these but in one case the red cell count was as low as 980 000 and the haemoglobin 20 per cent. Lymphocytosis and slight degrees of eosinophilia occurred in some 70 per cent. of the cases. Occasionally biochemical changes were noted in the blood—these consisted in a decrease of the total protein and a lowering of the albumin-globulin ratio but the author carefully states that as biochemical examinations were made only in the more severe cases the figures which he gives are not representative for the whole series. In a complete statistical study of unselected cases the figures would undoubtedly be different. Two patients had severe haemopoietic disturbance and one of these died. A blood culture after death revealed the presence of haemolytic staphylococci and streptococci. A full account of the post mortem findings is given and the full diagnoses are summarized thus—

(1) Lichen planus (New Guinea) (2) aplastic anaemia (3) focal myocardial hemorrhages and necrosis (4) bilateral pleural effusion (5) pulmonary edema (6) congestion of spleen (7) hepatitis subacute (8) bilateral pelvic hemorrhages in kidneys (9) subarachnoid and intraventricular hemorrhages (10) hypoplasia and fatty change of bone marrow (11) multiple ecchymoses of skin, voluntary muscles, diaphragm and viscera.

The lesions found in the liver were regarded as being of special interest—they consisted in subacute hepatitis characterized by degeneration of liver tissue and accumulation of chronic inflammatory cells. "In addition isolated masses of pigment were found which were non-negative and melanin positive (Becker stain). The Kupffer cells also contained large amounts of pigment. It is assumed that this pigment is bile pigment. However there is some resemblance to the melanin pigment of the skin.

With ultraviolet light the liver showed a marked greenish fluorescence. The presence of this marked fluorescence in a pathologic liver of a patient who had not had atabrine (mepacrine) for 6 weeks prior to his death again called attention to the possibility of atabrine being a factor in this disease. Since however this is the only case that I have seen, no definite conclusions are warranted.

The author concludes by stating: "It still is not clear why this condition should occur proportionately much more frequently in New Guinea than other

regions where similar conditions prevail. It is possible that atabrine is only one of the factors in a chain of causes which may eventually be found in diet, climate, ingested drugs insecticides or infection with malaria.

R M B MacKenna

ERRECART L. M. Sobre veinticinco casos de esporotricosis en el Departamento de Flores. [Twenty-Five Cases of Sporotrichosis in Flores.] *Arch Uruguayos de Med., Ciruj y Especialidades* 1946 Mar v 28 No 3 249-53 English summary

The author diagnosed twenty-seven cases of sporotrichosis during fourteen years. He thinks that sporotrichosis is a frequent disease not only in Flores but also in the other localities of Uruguay. No one lesion of the lungs was observed. Twenty six cases were localized in the upper limbs and one in a leg. All patients were males.

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## HEAT STROKE AND ALLIED CONDITIONS

MACKWORTH N. H. Effects of Heat on Wireless Telegraphy Operators Hearing and Recording Morse Messages. *Brit J Indust. Med* 1946 July v 3 No 3 143-58 9 figs [Summary appears also in *Bulletin of Hygiene*]

The decline in the capacity for manual work caused by exposure to high air temperatures especially in humid atmospheres has long been recognized. It is a matter of common experience that one's inclination for mental effort may diminish in very hot environments but the effects of heat on the capacity for mental work have not hitherto been clearly demonstrated experimentally. That is probably due to the experimental arrangements employed in some of the earlier investigations for in those studies different types of tests were used during any particular work-spell so that at intervals of 20 or 30 minutes there was a change of activity which introduced the powerful stimulus of variety. Many tasks are monotonous rather than variable and to assess the influence of temperature on the performance of such tasks protracted experiments are necessary. Such experiments were performed in the research described in this important paper with the result that a diminished performance in very hot environments was clearly shown.

The research was carried out on behalf of the Medical Research Council's Royal Naval Personnel Research Committee. That Committee wanted to know whether high temperatures affected some forms of human activity more than others so that it could be ascertained whether certain compartments in H.M. ships should have priority in the allocation of air-conditioning equipment and further it was desired to learn the extent of the overlap between the physiological effects of heat and the effects of heat on human performance as measured by psychological experiment.

In the study here reported the performance of eleven physically fit wireless telegraphy operators was examined. Before the main tests they were acclimatized by exposure to effective temperatures of 87.5°F to 89°F for three hours a day five or six days a week over a period of seven to eleven weeks. On the test days work was done for three hours during which period nine messages each of 250 groups, were transmitted at a speed of 22 words per minute. That is to say messages were transmitted for about 16 minutes with 3-minute intervals between messages.

The wind velocity was 100 ft. per min. throughout the series of tests, the dry-bulb temperature on different days was 85° 90° 95° 100° or 105°F., and in each instance the wet-bulb was 10°F. below the dry-bulb temperature. These conditions represented effective temperatures of 79° 83° 87.5° 92° and 97°F. Rectal temperatures were measured at the beginning and end of each work-spell. The men wore gym-shoes and white drill shorts and wrote the morse messages while seated at a table. There was plenty of unsalted water for drinking and each had a daily ration of 10 gm. of salt in addition to the ordinary dietary intake. During the run of the experiments the men had no exact knowledge of the accuracy of their performance on a particular day.

The main conclusions drawn from this investigation are —

1 Hot and moist atmospheres seriously impaired the accuracy with which these trained men could record morse messages heard over their headphones.

2 A statistically significant reduction in their accuracy first appeared when they were exposed to an effective temperature of 87.5°F. (with 85°F. dry bulb and 83° wet-bulb temperature). It had earlier been observed that most wireless telegraphy ratings in the Eastern Fleet had to work at effective temperatures of more than 84°F. and that conditions were worse during prolonged spells at action stations.

3 Hot and moist atmospheres raised the rectal temperatures.

4 Rectal temperature did not give even an approximate idea of the accuracy of work at wireless telegraphy reception.

5 Hence raised body temperature did not cause deterioration in ability to receive wireless signals, within the range of atmospheric conditions encountered by ratings in the Eastern Fleet.

It was noteworthy that the exceptionally competent members of the group were less affected by the difficult atmospheric conditions than men regarded as very good operators. Men of ordinary ability showed the greatest deterioration of all. [This is an interesting point. Other studies of industrial fatigue have shown that the more competent workers show less sign of fatigue than their fellows.]

There were no signs of cumulative effects from day to day but during a 3-hour spell the number of errors per hour rose progressively. Commonly errors were twice as numerous in the second hour as in the first and three or four times as numerous in the third hour. Severe head colds increased the rate of this falling-off in accuracy.

Thomas Bedford

### MISCELLANEOUS DISEASES

MANSON BAHK P. Some Tropical Diseases in General Practice. "A Post War Legacy" *Glasgow Med J* 1946 May v 27 No. 5 123-30

In this lecture Sir Philip Manson-Bahr reviews briefly the experience of certain tropical diseases as they affected the troops in the recent war and its predecessor and as they may affect practitioners in Britain who are faced with the difficult questions of diagnosis and treatment of those cases of, to them, uncommon and baffling complaints. He brings the experience of a lifetime to the evaluation of the important features noting that problems now sometimes regarded as new are, in fact, repetitions of those which arose 30 years ago. The sequelae of amoebiasis for instance, are rightly regarded seriously but after the war of 1914-18 it was found that the disease gradually petered out and no doubt this will happen again in the meantime effective treatment is by no means impossible and it is important to avoid the amoebiasis neurosis

Malaria has been controlled during the war more effectively than ever before and treatment is now very good. Although it is a correct attitude of mind to think first of malaria in soldiers who return from the East, a too facile diagnosis of enlarged spleen as due to malaria may lead to serious errors. The enlarged spleen usually retracts and disappears after one year's residence in a temperate climate, and in such patients some other cause should first be sought.

Sprue is still a mystery, the author favours the view that it is due to some infective agent. In treatment careful dieting and nursing are needed, but injections of crude liver extract are very useful. *Charles Wilcocks*

McCoy, O. R. Precautions by the Army to prevent the Introduction of Tropical Diseases. *Amer J Trop Med* 1946 May, 26 No 3 351-5

In this address to the Annual Meeting of the American Society of Tropical Medicine in November 1945 Colonel McCoy considers the problems arising from the return of troops from tropical theatres of operation to the United States.

He begins by pointing out that high standards of preventive medicine have been enforced among troops overseas and that troops in endemic areas have been immunized against such infections as yellow fever, cholera and plague.

Malaria has been the greatest disease problem and the author reveals that between December 1941 and June 1945 there were 430 000 hospital admissions for malaria in the U.S. Army.

Steps taken to minimize the hazards of malaria recurring when soldiers return to the United States include a co-ordinated mosquito control organization, continued suppressive medication for 28 days after arrival in the United States, and examination of the man and his blood before demobilization if conditions indicate it.

Colonel McCoy goes on to discuss the problems of dysentery, dengue, sand fly fever and scrub typhus. The hazard from dengue is the greatest and stringent *Aedes* control is essential at Army bases and airports. The possibility of the introduction of *Ancylostoma duodenale* is discussed. This species presents a greater problem than *Necator americanus* because it is more harmful, more resistant to climatic conditions and less amenable to treatment. Other helminthic diseases are also mentioned. General quarantine measures have been improved and strengthened, and a joint Army, Navy and Public Health Service Quarantine Board has been set up, and this Board takes advantage of the facilities for immunization and supervision exercised over members of the Forces.

The problems and the measures designed to deal with them are on orthodox lines, and the paper contains little that is original for the British reader. The relative urgency of the problem is underlined by two local factors: firstly, that American citizens have been spread over a larger area of the tropics and exposed to greater hazards of disease which is indigenous there than ever before in their history; secondly, that conditions in certain parts of their vast Continent are favourable to the maintenance and dissemination of some tropical diseases which would not flourish in more evenly temperate climates. The urgency is therefore more obtrusive to United States health legislators than to our own.

*H. J. O'D. Burke-Gaffney*

TRENCHARD, H. J. Inability to work in a Tropical Climate. *Brit. Med. J* 1946 Sept. 21 416-18.

This paper discusses the factors in invaliding between October 1944 and September 1945. 373 Royal Air Force men, chiefly ground staff, found unfit for

duty in South East Asia although not necessarily unfit for further military service in the United Kingdom.

The age of the men varied from 18 to 47 the majority being between 20 and 30. Most had been in the R A F between two and five years and their service overseas varied from 2 to 51 months the incidence of invaliding excluding that due to tropical diseases showed peaks during the first twelve months and after eighteen months of service overseas.

The principal causes of invaliding were—injuries 50 organic diseases excluding pulmonary tuberculosis which was not dealt with at this centre 178 and psychological abnormalities 147. The majority of the invalided were fit enough to travel by normal troop arrangements only 60 of whom 18 had injuries requiring transport by hospital ship.

Of the surgical cases the injuries formed an important proportion although only five were directly due to enemy action while of the surgical diseases disorders of the urinary system particularly calculus were noteworthy.

There were 50 patients with skin diseases of whom 10 had trouble before going overseas and the commonest conditions were epidermophytosis 12, and seborrhoeic dermatitis 12.

Tropical diseases accounted for 59 invalidings of which 34 were due to sprue and 15 to amoebiasis only 2 patients were invalided with malaria a low figure thought to be due to the efficiency of mepacrine suppression. The main causes for repatriation in amoebiasis were amoebic hepatitis persistent relapses of bowel infection and the development of a pre-sprue type of condition.

Of psychological abnormalities anxiety state was diagnosed in 86 patients hysteria in 33 psychoses mostly schizophrenia in 15 and psychopathic personality in 11. The principal precipitating factors of the anxiety neuroses appeared to be family or financial worries infidelity of the wife or discomforts of overseas service but in 15 cases no outstanding factor could be discovered. In those suffering from hysteria the precipitating cause appeared to be a subconscious desire to return home while the principal symptoms were headaches depression dizziness or dyspnoea. A feature of the psychotic patients and those diagnosed as being of psychopathic personality was the length of time that they were able to serve overseas before requiring invaliding some carrying on for more than two years.

F. Murgatroyd

HUTCH R. Some Advances in Medical Treatment. *J Indian Med Ass.* 1946 June 15 No 9 308-12 '39 refs

This is a succinct but useful review in which modern work on the sulphonamides penicillin streptomycin prostigmine nicotinic acid pyridoxine thioracil and the anti-malarial drugs is summarized. Sulphadiazine has almost supplanted the other compounds of the series and the author noting its efficacy in bacillary dysentery remarks that there is no reason why it should not be equally effective in cholera. He gives concise information on the use of penicillin in gonorrhoea according to the most recent work available. The story of the Australian work on mepacrine and Paludrine is briefly recounted.

Charles Walcock

FEIGENBAUM, A & KORNBLUTH W. Behcet's Disease as Manifestation of a Chronic Septic Condition connected with a Constitutional Disorder. With a Report of Four Cases. *Acta Med Orientalis (Palestine & Near East Med J)* 1946 Mar 5 No 5 139-51 [Numerous refs.]

The authors present a very clear account of this peculiar disease which is characterized by ulcers in the mouth and on the genitalia with eye lesions—

hypopyon irido-cyclitis retinitis optic neuritis—and by an eruption like that of erythema nodosum. Though cases have been reported from time to time since the end of the last century little if anything is known concerning the aetiology or pathogeny and treatment is far from satisfactory. Sometimes one or more of the symptoms mentioned above is absent. Partial cure seems to occur spontaneously in some cases but relapses come on after intervals of varying length perhaps 6-7 years.

Four cases are detailed in this paper three males of 24 25 and 28 years and one female of 25 years. One man died with nervous symptoms headache dizziness and convulsions the woman left hospital and could not be traced two improved. *Staphylococcus aureus* was cultivated from the lesions and the syndrome is thought to be due to a chronic septic condition in persons pre-disposed by in most cases latent tuberculosis trauma playing a part and possibly a large part in the primary localization of lesions. Though improvement in the general health takes place in non fatal cases it will be obvious from the severity of the eye symptoms that the damage to the sight may be great and permanent. Treatment by sulphonamides and penicillin and by injection of autogenous vaccines has been tried in some with apparent benefit but it is thought that the dosage may have been inadequate. The authors have given a helpful review of the literature of the subject and a very full list (two complete pages) of references to this interesting condition. [See also this *Bulletin* 1944 v 41 780 1946 v 43 157] *H Harold Scott*

RAO V G Some Observations on Cases of Ascites in Hyderabad-Deccan.  
*J Indian Med Ass* 1946 May & June v 15 Nos. 8 & 9 254-62 295-300 [59 refs.]

Among 343 consecutive cases of ascites admitted to the Osmania Hospital in two years there were 52 in which no definite organic disease was detected these are classed as being due to nutritional deficiency. Most of the 52 were young or middle-aged adults of the labouring class whose diet provides sufficient calories but is of poor quality and deficient in protein. Although there were approximately equal numbers of the two sexes in the general admissions to hospital 46 of these 52 cases of nutritional ascites occurred in males. In some patients the ascites was accompanied by pleural and pericardial effusions and by anaemia of moderate degree. Serum proteins were determined in 8 patients in 7 of whom the ratio of globulin to albumin was greater than 1.

The majority of the patients recovered with rest in hospital and on a diet more liberal and better balanced than that at home. Complete disappearance of the ascites followed by gain in real weight was obtained in 32 cases and the condition of 10 others was improved. Seven patients died.

Only a few patients were followed up after leaving hospital. 15 were known to be in good health for periods varying up to 2 years. Four patients who were classed as having 'nutritional ascites' and who were discharged after clinical recovery returned later two with cirrhosis of the liver one with pulmonary tuberculosis and one with pleurisy.

The second part of this paper records the findings in the 108 cases of portal cirrhosis included in the 343 cases of ascites. The condition appears to be common in India but apart from a suggestion that defective diets play some part there is no evidence to explain its etiology. Twenty of the 108 patients were vegetarians and total abstainers because of their religion and from only 40 of the remainder could a history of occasional 'toddy' or 'sundhi' drinking be obtained. (The alcoholic content of these drinks is only about 7 per cent.)

Bleeding was uncommon in these patients—only one had haematemesis three had melæna, and five had bleeding piles. Examination of a few cases showed moderate anaemia, and low serum proteins with a reversed albumin/globulin ratio. Response to treatment was unsatisfactory and unlike the patients with nutritional ascites many of the patients died in hospital while most of the remainder showed little improvement after repeated paracenteses.

It is suggested that cases classed as nutritional ascites may at first be due to simple malnutrition without gross hepatic lesions and may be capable of recovery but that a continued state of malnutrition may ultimately result in a fully developed picture of portal cirrhosis.

H. E. Harding

BECKER B. J. P. Cardio-Vascular Disease in the Bantu and Coloured Races of South Africa. I. Incidence, Pathology and General Features. *South African J Med Sci* 1946 Apr v 11 No 1 1-14 3 figs [13 refs.] II. Congenital Heart Disease *Ibid* 15-17 [10 refs.] III. Rheumatic Heart Disease. *Ibid* 18-34 1 fig [43 refs.]

These three papers, or sections of one contribution, are excerpts from a doctorate thesis. They comprise an analysis of those among 3,000 autopsies performed at the Johannesburg General Hospital during 14½ years ending June 1938 showing cardiac or cardio-vascular disease. Some 12 per cent. of Bantus and coloured persons were found to have died from circulatory disease a proportion about the same as that recorded in other parts of the world.

For the purpose of his analysis the author uses the following classification: Congenital and Acquired, 2.5 and 97.5 per cent. respectively and the latter he subdivides into three main groups: Inflammatory which includes rheumatic, syphilitic and tuberculous; Metabolic and Physical which includes atheroma, arteriosclerosis and beriberi; and, thirdly Neoplastic—a classification not altogether satisfying.

Among the 3,000 there were 1,335 or 48 per cent. showing some disease of the circulatory system. As regards sex, 1,041 occurred among 2,180 males autopsied (47.5 per cent.) and 344 among 810 females (42.5 per cent.) so that sex differences are negligible. No indication was found of any special racial susceptibility among the seven races making up the total.

Atheroma was the commonest lesion found and next to this, hypertensive heart disease but in the majority these were not the sole lesions. Tuberculous disease of the heart was found in 4 per cent. of those dying under 30 years of age and in 6 per cent. of those over 30 years. Syphilitic disease was less in evidence in only 2 per cent. below 30 years and in 6 per cent. of those over 30 years.

As regards valvular lesions, there were 108 cases of aortic incompetence among the 3,000 autopsies (3.5 per cent.) 57 (1.8) of mitral stenosis, 16 (0.5) of aortic stenosis, and 5 (0.2) of mitral incompetence. There were 51 cases of aneurysm, most due to syphilitic aortitis and 37 of the patients died from rupture of them.

In the second paper the author records that there were 35 cases of congenital heart disease among the 3,000 (1.18 per cent.) excluding abnormalities of the vessels, hypoplasia and aneurysm, and displacement due to primary diaphragmatic deficiency; this figure is reduced to 13 (0.4 per cent.) Infective endocarditis was found in two only of these congenital cases.

In the third paper rheumatic heart disease is discussed in more detail. One hundred and six such (3.5 per cent.) were found among the 3,000. It was most common in the 11-20-year group constituting 10 per cent. of the autopsies and 33.7 per cent. of the cardiac cases. Among females with organic heart disease "rheumatic heart" was present in 15 per cent. among males 5 per cent. but the variation in females is stated to be 5.3-24.5 per cent. and in

males 15-85 There is thus says the author no significant difference [a conclusion not easy to follow] For this analysis the author classifies rheumatic heart disease into three main groups Acute rheumatic carditis latent (developing) carditis and developed lesions. These are each of them further sub-divided and discussed Space forbids more detailed account here those interested should consult the original paper or better still the complete thesis if it is published Suffice it here to say that the mitral valve was involved alone in 38 and together with other lesions in 42 or 80 in all The aortic valve alone was involved in 23 In about one-third of the cases of rheumatic heart disease bacterial endocarditis was superimposed the aortic valve was affected in this way more often than the mitral and both together in four Among the author's conclusions two are particularly striking First In its age and sex incidence among Bantu and Coloured races it [rheumatic heart disease] cannot be said to differ in any essential way from the condition as seen in other parts of the world secondly There is a somewhat higher incidence of bacterial endocarditis in Bantu and Coloured subjects in association with rheumatic valvulitis than occurs in other parts of the world [The whole is an interesting and painstaking study ]  
H Harold Scott

D ARCANGELO D Le cardiopatie nei nativi dell'Eritrea (Considerazioni etimopatogenetiche clinico-statistiche) [Heart Disease in Eritreans.] *Boll Soc Ital di Med e Igiena Trop* (Ser. Eritrea) 1945 v 5 Nos. 5/6 231-46 [42 refs.] English summary (4 lines)

STEPHAN E Tropical Eosinophilia in Egypt. Report of a Case *Lancet* 1946, Aug. 17 236

GOLDSTEIN B Two Cases of Disseminated Sclerosis in African Natives. *East African Med J* 1946 June v 23 No 6, 170-73

BUFFA F & D ARCANGELO D Sui casi di cancro del laringe osservati in Eritrea (contributo clinico-statistico) [On Cases of Cancer of the Larynx in Eritrea.] *Bull Soc Ital di Med e Igiena Trop* (Ser. Eritrea) 1945 v 5 Nos. 5/6, 135-49 [24 refs.] English summary (4 lines)

## GENERAL ENTOMOLOGY

TERMINAEV P P [Flying Activity and Attack on Man of Various Species of *Anopheles* and *Culex* under Natural Conditions in Uzbekistan.] *Med Parasit & Parasitic Dis* Moscow 1945 v 14 No 5 15-35 11 figs. [In Russian.]

The author records the results of observations upon the flying activity and attacks upon man of mosquitoes carried out chiefly among the rice fields of Uzbekistan from March to October of the years 1939-1943 The study was restricted to *Anopheles* and *Culex* (*Anopheles maculipennis sacharovi* *A. hyrcanus* *A. claviger* (*bifurcatus*) *A. superpictus* *A. pulcherrimus* *Uranotaenia theobaldi* *A. longiareolata* *T. annulata* *Mansonia* *Aedes caspius* *Aedes detritus* *Aedes pulcherrimus* *Aedes vexans* *Culex*)

Counts were made by using a trap constructed as follows a sheet was suspended on four poles, with the edges touching the ground one side of the sheet being raised during the observations to form an inlet for the mosquitoes. One or two men who served to attract the insects and remained under cover of



this tent with a lamp burning all night made observations on and collected the mosquitoes, keeping hourly records of temperature, humidity and wind. When flight ceased the sheet was removed.

The results shown in numerous tables and charts were as follows: among the Anophelinae and Culicine mosquitoes entering the tent unfed females formed 87 per cent. those with blood in the stomach 8.4 per cent. those with developed ovaries 2.3 per cent. males were 1.7 per cent. The maximum number of attacking mosquitoes was observed in July constituting 38.2 per cent of a total number of actively attacking mosquitoes during the whole season. The minimum density was in April (1.5 per cent.) in May (2.6 per cent.) and in October (3.1 per cent.). The temperature limit at which activity was highest was 33.5°C. while at 9°C it was lowest the temperatures being between 15° and 25°C in May and 11–15 in October with intermediate values in September and April. As regards humidity it was found that 100 per cent. relative humidity had a depressing effect upon the activity of mosquitoes. The insects manifested a positive phototaxis to the weak source of artificial illumination while sunlight at temperatures not exceeding 20°C had no inhibiting effect. However high temperatures combined with intensive insolation and evaporation were unfavourable the mosquitoes keeping to their day shelters under these conditions. The mechanical and denaturing action of wind proved to be of primary importance. The maximum speed of wind at which flight of mosquitoes took place was 4.17 metres per second when the speed does not exceed 2 m/sec they fly in the open air above this speed they fly low in the grass. The daily rhythm in the attacks of mosquitoes corresponds to periods of evening and morning maxima, and night and afternoon minima of flying activity. During the maximum evening periods the first mosquitoes to attack are *Aedes caspius* and *Culex* the density of which increases progressively from sunset to night after which it declines while the density of *Anopheles* begins to rise.

C. A. Hoare

MARA L. Considerazioni sul rinvenimento dell' *Aedes aegypti* L. (*Dip. ardians*) ad altitudini eccezionali e brevi note sulla fauna culicidica del Mt. Bizen (Eritrea, A. O.) [A Note on the Finding of *Aedes aegypti* at an exceptional Altitude with a Short Note on the Culicid Fauna of Mt. Bizen.] *Boll. Soc. Ital. di Med. e Ig. Trop.* (Sex. Eritrea) 1945 v. 5 No. 5/6 189–98. [16 refs.] English summary

In this note it is said that *Aedes aegypti* L. has been found on the Bizen mountain (Eritrea, East Africa) at the exceptional altitude of 2,400 metres above sea level. This altitude is 450 metres higher than that previously quoted by other authors in Kenya Colony (1,950 metres above sea level).

WISSEUP C. B. BROTHERS W. C. EIDZ P. M. & DEONIER, C. C. DDT Emulsion applied to Rice-Field Water to control Mosquitoes. *J. Econom. Entom.* 1946 Feb. v. 39 No. 1 52–5

The authors' object was to run DDT emulsion into irrigation water in the channel before it flowed on to the rice field thus attaining distribution through the mechanical flow of the water. The stock concentrate consisted of 20 per cent of DDT 20 per cent. of *Triflow X 100* a proprietary emulsifier and 60 per cent of xylene this was diluted with water before application by means of a drip can.

Concentrations of DDT of less than 0.1 part per million gave very limited control. Doses of 0.2 p.p.m. and 0.4 p.p.m. gave control of breeding in fields near to the channels on which the treatment was applied, but not in the more

distant fields. A dose of 0.6 p.p.m. gave complete initial control and residual control was noted in some cases. It is concluded that the degree of control depended on (a) the concentration of the DDT emulsion in the water (b) the dosage of DDT per acre (c) the distance that the emulsion was carried in the channel before it entered the field and (d) the size of the field. Subsequent laboratory tests have shown that intense aeration of water containing DDT causes a decided loss of toxicity to mosquito larvae.

There was no noticeable damage to the rice and no decrease of plump grains in the treated fields. The mosquitoes concerned were *Anopheles* and *Psorophora*.

G Macdonald

CALIFORNIA MOSQUITO CONTROL ASSOCIATION. Proceedings and Papers of the Fourteenth Annual Conference of the California Mosquito Control Association held at Agriculture Hall, University of California, February 25 & February 26, 1946. 115 mimeographed pp. 2 figs. [\$1.50]

This is an account in 115 pages of a conference of the California Mosquito Control Association held in Berkeley, California in February 1946.

It includes 19 technical papers and 3 reports on field work in different districts and covers a wide range of material largely concerning the use of DDT in malaria control. There is a full account of the discussions which took place during the Conference.

To appreciate the background of this Conference and the significance of the subjects discussed the original *Proceedings* should be studied.

H J O D Burke-Gaffney

JAYEWICKREME S H & NILES W J. Successful Feeding Experiments with an Adult Trombiculid Mite (Order Acarina) [Correspondence.] *Nature* 1946 June 29 878

Although nearly all workers interested in scrub typhus have tried to breed the trombiculid mites which are believed to transmit the rickettsia little success has previously been achieved. We know that the larval stage must feed on a vertebrate host (viz. a rat) but the nymph and adult living in the soil have given more difficulty and their food has not been recognized. A few have on occasion been reared in various media but it has been obvious that the proper diet has not been discovered. MITSUDA and OKUMURA state that *Trombicula akamushi* lives on plant juices but other workers have not confirmed this.

The authors of this communication have for the first time discovered a satisfactory diet for nymphs and adults. They found *Trombicula aculeolaris* larvae parasitizing rats and bandicoots and obtained adults and nymphs crawling on the vegetation choking a pond in which the mosquito *Mansonia uniformis* was breeding. The adult and nymphal mites were found to attack *Mansonia* eggs with avidity and also to feed on *Anopheles* eggs. This mite is clearly carnivorous in its adult and nymphal stages.

Kenneth Mellanby

WHARTON G W & CARVER R. L. Food of Nymphs and Adults of *Neoschöngastia indica* (Hirst 1915). *Science* 1946 July 28 76-7

This investigation was very similar to that described by Jayewickreme and Niles (above) but the mite *Neoschöngastia indica* was used. The adults and nymphs were found to feed readily on mosquito eggs and on other insect eggs. They were also noticed to be cannibalistic so this species also is clearly carnivorous.

Kenneth Mellanby

WILLIAMS, R. W. The Laboratory Rearing of the Tropical Rat Mite, *Liponyssus bacoti* (Hirst) *J Parasitology* 1946 June v 32 No 3 252-8, 4 figs.

Work on the transmission of filarial worms in the laboratory has generally been difficult owing to the lack of a suitable arthropod vector. *Liponyssus bacoti* the tropical rat mite is an intermediate host of the filarid *Litomosoides carinii*. This mite is common in the United States, and is easily reared in the laboratory. An artificial rats' nest is made by placing loam soil half an inch deep in a box and a layer of straw above the soil. Rats (either cotton rats or ordinary albinos) in small cages are placed in the box over the straw and soil. The whole arrangement is then stood in a tray of water to prevent the mites from escaping. The soil and straw provide a suitable harbourage for the mites and absorb the rats' urine the production of which is kept at a minimum by giving no water to drink. A high humidity over 70 per cent. (preferably 85-90 per cent.) is recommended [it must approach saturation among the soil and straw]. A room temperature of 21°C. gives good results [again the mites will be in a different warmer micro-climate]. The mites receive no special attention except to ensure that the straw does not become too damp. One such culture started with 32 mites and in a fortnight numbered over 1 000. The female mites lay about 7 eggs after each blood meal they feed approximately every second day. The eggs hatch in two days to give a six-legged larva which moults without feeding in about 24 hours. Breeding is said to be so prolific that the host rats may die from anaemia. [*Liponyssus* might also be used in the laboratory for work on the transmission of murine typhus. It has been shown to be a vector of this rickettsia, in *Rev Applied Entom.* Ser B., 1932 v 20 49.]

Kenneth Vellaby

WHARTON, G. W. & HARGREAVE, A. B. The Genus *Neoschöngastia* (Acarinida: Trombidulidae) in the Western Pacific Area. *J Parasitology* 1946 June v 32, No. 3 288-322 15 figs. [16 refs.]

"1 The genus *Neoschöngastia* Ewing 1929 is redefined.

2. A key to the species of *Neoschöngastia* found in the Pacific area is given.

3. Eleven new species and one new subspecies of larval *Neoschöngastia* are described.

"4 Two nymphs of *Neoschöngastia* are described and a diagnosis of the genus on nymphal characters is given.

DELPHY, L. P. Revision par des notes expérimentales du genre *Hyalomma* C. L. Koch 1844 (*Acarina Ixodidae Ixodidae*). Note préliminaire. [Experimental Review of the Genus *Hyalomma*. A Preliminary Note.] *Arch Inst d'Histoire Nat.* Teheran, 1946 Jan v 2, No 2, 61-63, 2 figs & 1 folding pl. [21 refs.]

WELSH, J. H. & SCHALLER, W. Arthropod Nervous Systems: a Review of their Structure and Function. *Phys & Rev* 1946 July v 26 No. 3 447-78. [Numerous refs.]

## LABORATORY PROCEDURES.

ROGERS K B Oil Sterilisation of Syringes. *Lancet* 1946 July 20 87-8.

The need for scrupulous sterilization of syringes and needles has been widely discussed of recent years and the need is heightened by the recognition of the possibility that non-sterile instruments may transmit infective hepatitis.

Sterilization by hot oil was advocated as long ago as 1921 by WRIGHT and COLBROOK in their *Technique of the Test and Capillary Glass Tube*.

The author recommends that immediately after use the syringe should be rinsed in water and thus freed of blood. The needle is then removed and the syringe filled three to four times with liquid paraffin at 130° to 140°C. with a second pause at each filling. The needle is replaced and the oil again sucked in and expelled. The sterile syringe is kept in place in a test tube by means of a folded strip of plaster.

The method has the advantage of speed and there is no risk of haemolysis. The heat of the oil should not exceed 150°C as the cement holding the glass to the metal parts may melt. With larger syringes the piston may jam owing to cooling and contraction of the glass but it moves freely again within five minutes. Syringes treated in this way are not sterile on the outside and are thus unsuitable for operating-theatre purposes but are satisfactory for ordinary injections. Oil sterilization does not kill spores contained in dried blood.

The author describes five experiments in support of the oil sterilization method. Cultures of staphylococci streptococci *Bact coli commune* and *M tuberculosis* contained within syringes or in blood which has infected syringes were sterilized by from one to four fillings of oil at 120° to 140°C. Syringe barrels and pistons containing dried blood infected with *Staph aureus* were sterilized by two minutes immersion in oil at 120°C.

Blood containing spores of *B subtilis* was dried in syringes the spores were not killed after 12 minutes in oil at 120°C.

[It is not quite clear why the spores of *B subtilis* were not exposed to the higher temperature ranges before it was concluded that they were not killed by oil sterilization.]

H J O D Burke-Gaffney

LERNER E M A Rapid Gram Stain for Tissue *Arch Pathology* 1946  
June v 41 No 6 674-5

The author describes a modification of the Gram stain for the demonstration of bacteria in tissues which he claims overcomes the complications of time labour and inadequate differentiation inherent in the recognized modifications. The method requires less than five minutes of actual staining time and it is claimed gives excellent morphological detail. Bacteria stand out sharply and spore-bearing organisms are recognized readily.

Paraffin sections of Zenker fixed tissues are heated at 56°C. for two to six hours. The actual staining is essentially that of the Gram method for bacterial smears consisting of the conventional crystal violet iodine solution acetone-alcohol, and 1 per cent. safranin as a counterstain. Detailed steps in staining are described in the original paper.

H J O D Burke-Gaffney

DUNN R C A Hemoglobin Stain for Histologic Use based on the Cyanol-Hemoglobin Reaction. *Arch Pathology* 1946 June v 41 No 6 676-7

A cyanol-peroxidase reaction is described which has been found by the author to be highly specific for haemoglobin in paraffin sections of tissue fixed

in 4 per cent. solution of formaldehyde buffered to pH 7.0. The specificity and sensitivity of cyanol as a haemoglobin stain is equal to that of patent blue V in most instances. The actual staining time is about ten minutes. By this method haemoglobin stains blue to bluish grey.

The technique of this method is described in detail.

*H J O'D Burke-Gaffney*

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## REPORTS SURVEYS AND MISCELLANEOUS PAPERS.

### INTERNATIONAL LABOUR REVIEW 1946 Mar-Apr v 53, Nos. 34 194-9 Land Aspects of Labour Problems in Kenya.

In the Kikuyu territory of South Nyeri Kenya the population is increasing at the rate of 2 per cent per annum. The actual amount of land available was no more than 3.35 acres per family in 1944 which would be reduced to 2.61 acres in 1955: this is insufficient for subsistence. Other land is therefore sought largely by tenant farming, but for various reasons there is little inducement for the tenant farmer to conserve land from which he may be evicted at any time. To augment their income men seek paid employment away from their homes leaving their wives to carry out all home farming and the collection of fuel, which often involves long trips and the carrying of loads sometimes more than 200 lb in weight. These women are fast becoming mere drudges.

The solution of this problem lies in part in removing a large proportion of the population from the land, and creating a wage-earning group which involves provision for the housing not only of the men, but of their families at the places of employment. The general land policy envisaged by the Government of Kenya aims to check soil erosion, to secure the proper use of water and timber resources and to encourage efficient agriculture. "It is on the general standard of living of the people even more than on the development of production for export that the economic progress of the colony as a whole must primarily depend. Co-operative farming cannot be undertaken without elaborate preparations—fencing, clearing, provision of water supplies and adequate housing. Moreover financial help, technical guidance and control by Government are essential before the African adopts effective methods. The natural tendency is towards over-cropping, over-stocking with useless cattle, under-fertilization and failure to conserve the resources. The two important factors are soil-conservation and water supplies and a scheme to deal with these matters has been approved in principle: this will cost £60 000 in the first year and £600 000 in ten years. It is however realized that greater sums than these will be needed, but it is also known that the effort and expenditure are essential to relieve the over-populated and over-stocked areas and to develop the country so that its people may be healthy and prosperous.

[The effect of these conditions on health are obvious and in Kenya, as in South Africa, it is evident that the interdependence of the various departments of government is appreciated. The story of the Anchan settlement in Nigeria is apposite in that many departments have collaborated to good purpose and that a large measure of control is necessary to overcome ingrained habits of inefficient farming which were of little importance when land was plentiful, but which are dangerous now.]

*Charles Wilcocks*

GALE G W Health Centre Practice Promotive Health Services and the Development of the Health Centres Scheme *South African Med J* 1946 June 22 v 20 No 12 326-30

The Health Centre system has been adopted as part of the Government plan for improving the health and medical services in the Union of South Africa [see this *Bulletin* 1946 v 43 498-501] and a centre has been in existence since 1940 at Polela, Natal [see this *Bulletin* 1944 v 41 611 1946 v 43 162]. The idea of Health Centre work is not merely to provide a service for those who attend because they are ill but to study all persons in the area, in their homes and by inducing them to come periodically for examination. Both preventive and curative services are provided but the Health Centres will gradually supplant the special clinics. The provision of this service will often if not always depend upon initiative exercised by voluntary agencies. At present there exist in the Union 8 of these centres 3 more are to be started in July 1946 and 9 others in October. Each has now one medical officer one to three nursing sisters and subsidiary staff but eventually there will be in each centre two medical officers a dental surgeon (part time) and increased staff in general. The training of the staffs is being undertaken partly at the former military hospital at Springfield Durban and partly in Health Centres in and around Durban. In June 1946 there were 16 medical officers and 60 health assistants in training.

These Health Centres will not only conduct their day to-day work on the lines indicated they will also be research centres free to conduct experiments to evolve new techniques and to adapt themselves to varying needs. The practice of social medicine and the study of all factors which bear on health will be within their sphere as is indicated by the paper by KARK and KARK to which reference has already been made [this *Bulletin* 1946 v 43 162]. [This work is admirably conceived and the future progress of these centres will be watched with the greatest interest]

Charles H Ilcocks

PALLEY A. & BRUWER, T. An Analysis of the Medical and Social Conditions of Native Children attending Groote Schuur Hospital Paediatric Out Patient Department. *South African Med J* 1946 June 22 v 20 No 12 339-41

The authors made an investigation into certain aspects of living conditions of 61 unselected African children who attended the paediatric out patient department of the Groote-Schuur hospital. Most of them were under 2 years of age and in most cases the father supported the children though some fathers had deserted their families the parents were interested in the health of their infants and even under adverse conditions were good parents. It seems probable that the infant mortality rate is much higher in these urban Africans than in the Europeans.

Only 42 of the children lived in brick houses the rest lived in shacks 38 houses were fit for human habitation the remainder not. In 34 instances the family (2-10 persons) occupied one room only for living and sleeping. In 45 families the fathers and in 13 the mothers were employed while their children were all the monthly income varied from nothing to more than £15 per month most families receiving from £5 to £10. The authors comment that for a family to exist on less than £10 per month means gross poverty yet 85 per cent of these families did so. Rent was usually up to £2 per month but in 10 families it was between £2 and £5 travel to work by train or bus was necessary for 36 bread winners.

Of these children no less than 21 were suffering from tuberculosis and 17 from other respiratory infections this fact is significant when considered in relation to the housing conditions and overcrowding.

An outstanding feature of the book is its vigorous and stimulating style. The author evidently believes that a book of this kind should provide interesting reading as well as accurate information: he has certainly succeeded in achieving this aim. At the same time he has remembered that his book is an introduction to parasitology rather than a text-book upon it. Emphasis has therefore been laid upon the biological aspects of the subject. We find, for example, that more space is devoted to life-histories, host-parasite relationships, epidemiological problems and to the principles of control and treatment which are based upon these, while relatively less is given to classification, morphology and nomenclature. Brief bibliographies at the end of each chapter introduce the reader to the vast literature on parasitology so that he can readily study in more detail those aspects of it which interest him. At the end of the book there is a list of the leading journals in which papers upon various aspects of parasitology appear and particular attention is called to the *Tropical Diseases Bulletin*, the *Veterinary Bulletin*, *The Review of Applied Entomology*, *Series B*, *The Journal of the American Medical Association*, *Biological Abstracts* and *Helminthological Abstracts*. "The six periodicals mentioned," says Chandler, "on account of their scope and thoroughness are of inestimable value to anyone who attempts to keep pace with the progress of parasitology."

Every parasitologist will heartily endorse this tribute to these invaluable sources of information. Many of them will wish to add a tribute to the value of this book of Chandler's. It is a considerable achievement nowadays to follow in detail and to assess accurately the advances in our knowledge of even one group of Protozoa, Helminths or Arthropods. For this reason, perhaps, some books on parasitology omit either the Protozoa or the Arthropods which are associated with disease and concentrate upon only two of these three phyla, to which most of the animals parasitic in man and his domesticated stock belong. It is therefore especially useful to have in this book an adequate treatment of all these phyla. The biologist too who wishes to relate our knowledge of animals parasitic in man and his domesticated stock to his studies of those parasitic species which have no economic importance will find in this book an admirable fusion of the biological and the economic points of view.

The book is well printed and handy to use. Some of the illustrations could be improved, but most of them are adequate and no doubt it is the author's intention that they should be supplemented by observations made upon actual parasitic animals which cannot be replaced by illustrations, however excellent these may be. There will be some readers nevertheless who cannot take laboratory courses in parasitology and the inclusion in future editions of some of the excellent photographs of parasitic animals which are now available would, no doubt, add to the value of the book. On the other hand, some teachers may prefer the line drawings with which this book is illustrated, because they cannot represent exactly the parasitic animal and therefore do not encourage the student to avoid making his own observations and drawings.

The book can be recommended to both the general public and to the biologist, who will be grateful to the author for guiding the earlier editions into this valuable fusion of readable text and accuracy of complicated information.

G. Lapage

NEVEU-LEMAIRE M. [Professeur agrégé des Facultés de Médecine] *Traité de Protozoologie Médicale et Vétérinaire*. [Treatise on Medical and Veterinary Protozoology] pp. xx + 844 433 figs. 1943. Paris: Vigot Frères Editeurs, 23 Rue de l'École-de Médecine. [45s.]

Like its companion volumes on Helminthology and Entomology (this *Bulletin* 1936 v 33 643 *ibid.*, 1933 v 33 631) this treatise on Protozoology

will undoubtedly be found to be a valuable and convenient book of reference. In fact the reviewer has already had occasion to consult it on several occasions and has obtained references which otherwise he would have had some difficulty in procuring. The book contains a vast amount of information on all aspects of medical and veterinary protozoology much of it taken from obscure sources which are not frequently consulted. But it is not up to date even if allowance is made for the fact that the date of the author's preface is 1942. Very little reference is made for instance to the developments in knowledge regarding avian and simian malaria and the many species of these parasites including *P. knowlesi* which have come to light in recent years are not mentioned. The importance of the exoerythrocytic cycle in malaria is passed over in a single line. One finds again the old statement that the sporozoite enters the red blood corpuscle. *P. ovale* is merely mentioned in a foot note as being of doubtful validity while little attention is given to the relationship of the three common human parasites to the similar forms in chimpanzees.

In general the reviewer finds that the book covers very much the same ground as his own *Protozoology* published in 1926 from which the author has borrowed many figures. The treatise under review however contains much that is not found in the reviewer's book. A considerable amount of space is devoted to consideration of symptomatology pathology treatment and prophylaxis of diseases due to protozoa. Over 120 pages are devoted to the intestinal ciliates of domestic animals and their relations—a proportion of the book which seems in excess of their importance. Nevertheless for purposes of reference the account will prove of use. Again under the heading *Treponema*—for as is the custom the spirochaetes and other non protozoal organisms encountered in blood work are dealt with—90 species are mentioned in most cases with reference only to the host. *Rickettsia* and rickettsial diseases receive 35 pages. Finally as in the companion volumes the book has a list of hosts and their parasites a list of intermediate hosts and vectors and a list of vertebrate reservoirs chiefly mammals. The book is well illustrated with 433 figures and finishes with a fairly good index.

C. M. Wenyon

DUBOIS A. *Chimiothérapie des trypanosomiases*. [Chemotherapy of Trypanosomiasis.] Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales. Mémoires (Collection in-8°) 1946 v. 15 No 7 169 pp [258 refs.] [100 fr.]

The scope of this volume is severely limited. Apart from a few introductory sections on general aspects of the chemotherapy of trypanosomiasis it deals in detail only with arsenicals and antimonials excluding any consideration of mechanisms of drug action or general theory. A second publication is projected to cover non metallic preparations and general theoretical considerations. In a prefatory note the author writes that the volume prepared during the German occupation served to support him during that painful period but that the circumstances prevented him from keeping fully abreast of recent literature. Certain additions and alterations will therefore be necessary but he has felt obliged to arrange for publication before making these changes because of a journey to Africa. He intends therefore to produce a supplement in due course to set matters right. Those who will wish to use this book will certainly feel that they would have preferred to wait until it could be presented in a more finished form. A number of misprints are corrected in a page of errata at the end of the book there is no table of contents and most serious of all there is no index. An index is of course essential in a work of this nature which is most likely to be used not as a book to be read from beginning to end but as a volume to which one will resort, from time to time in reference to a particular compound chemotherapeutic problem, or author.



The introduction reminds the reader that practice based on empiricism, has long preceded theoretical development in the field of chemotherapy (as for example, in the time-honoured use of cinchona bark, mercury etc.) The development of chemotherapy as an exact science was due in large part to researches on trypanosome infections. Whilst LINGARD and BRUCE before the turn of the century may be regarded as pioneers in the empirical chemotherapy of trypanosomiasis and LAFERAN and MESNIL (1902) were the first to embark on systematic experimentation EHRICH for his labours from 1903 to 1915 is undoubtedly to be hailed as the true founder of experimental chemotherapy. Apart from its outstanding theoretical value his work with trypanosome infections was an essential stage towards the triumphal announcement of the first sound cure for syphilis.

The author writes that his compilation is intended to be of particular service to Belgian colonial medical officers by placing at their disposal the facts known about preparations active against trypanosomiasis, both of man and of animals, and he then recalls with justifiable pride some of the unique contributions of Belgian workers towards the study of trypanosomiasis in the Congo. The Léopoldville laboratory founded in 1899 under the inspiration of General DONTY turned a major part of its attention to trypanosomiasis at its very inception with VAN CAMPENHOUT as the first Director. His successor BROUEN (1900-1911) together with RODRIGUE developed this interest still further. They conducted numerous field trials of compounds prepared by Ehrlich, and it was they who first introduced the practice of exhibiting tartar emetic intravenously in man. They were also pioneers (1908) in the evaluation of cerebrospinal fluid changes in sleeping sickness. MORCHET and DUBOIS (1911-1912) were among the first to embark on itinerant mass-treatment, now one of the principal methods of sleeping sickness control. MISS PEARCE and VAN DEN BRANDEN conducted the first field trials of trypanamide, and van den Branden, VAN HOOFF and others have subsequently investigated numerous other products and therapeutic procedures. Human trypanosomiasis which is the chief anxiety of the health service, remains at the present time in the forefront of the Léopoldville laboratory's activities.

The first section deals with general principles underlying the treatment of human trypanosomiasis under the sub-headings of "Intercurrent diseases", "General rules of treatment" and "Follow-up after treatment". There follows a section entitled "Methods of experimental chemotherapy" dealing with experimental procedures in laboratory animals and *in vitro* and including also a consideration of the normal course of infection in untreated human cases. A few pages follow to discuss busurth, gallium, indium, gold, rhodium and ruthenium, and the work then deals systematically first with arsenicals and then with antimonials.

The arrangement of material presented might perhaps be improved. For example an explanation of the term "Chemotherapeutic index" follows immediately on the section headed "Experiments *in vitro*" instead of being included in the section for "Experiments *in vivo*". Again, having passed on from a general and detailed consideration of arsenicals to a similar treatment of the antimonials one is then brought back to the arsenicals (with section-headings in printing type which would suggest that we are still among the antimonials) for accounts of intrathecal treatment, intracarotid treatment and ocular troubles after arsenical treatment.

Omissions and ambiguities are inevitable in a compilation of this nature especially when prepared under such inauspicious circumstances. It would therefore be ungracious to pick on these particularly when so much is reliably recorded. In any case, the wise reader will of course prefer in his hour of need, to go to the original sources, liberally indicated by the author who does not however

claim to give a complete bibliography and admits to giving special notice to the publications of Belgian workers. His lists together with those given in FINDLAY's *Recent Advances in Chemotherapy* (London Churchill 1939) will guide the reader to all important literature-sources up to the outbreak of the recent war. The most exhaustive lists of references up to about 1934 are probably those in FISCHL and SCHLOSSBURGER's *Handbuch der Chemotherapie* (Leipzig Fischers 1934).

Lest it be thought that this volume is received with unduly faint praise let it be said that we will welcome the second volume and will look forward to placing it on a near by shelf for easy access together with this one—all the more so if it is to include an index to the entire work.

E M Lowrie

FELSEN Joseph [B.A. M.D. Director of Medical Research, Bronx Hospital New York etc.] *Bacillary Dysentery, Colitis and Enteritis*. pp. xiv + 618 145 figs (2 coloured) 1945 Philadelphia & London W B Saunders Company [30s]

This book is a review of our knowledge of all the aspects (clinical pathological and epidemiological) of acute bacillary dysentery, chronic ulcerative colitis and distal ileitis. The author believes that chronic ulcerative colitis and distal ileitis are the late sequelae of acute bacillary dysentery and that their onset can often be traced to an attack of acute dysentery. This opinion is based on experience in the U.S.A. where the incidence of Flexner dysentery and of chronic ulcerative colitis appear to be very much greater than in Britain.

The sections dealing with the symptomatology, diagnosis and treatment of these conditions are clear and up to date. The use of the sigmoidoscope and X-rays in diagnosis and in the control of treatment is advocated and there is a clear account of the sigmoidoscopic findings and radiological appearances in dysentery, colitis and other disorders of the bowel. There is however no mention of the precautions to be taken during the nursing of acute bacillary dysentery either in hospital or at home to prevent the spread of the disease to other persons.

The epidemiological and bacteriological aspects of bacillary dysentery are less satisfactorily described. The author uses the historical approach and frequently quotes the experiences of other workers with too little regard for differences in methods and material. In this way parts of these sections have become merely a confused record of the conflicting findings of others. The description of the bacteriology of the *Shigella* group is no fuller than that given in the standard text-books and is made more confusing than is necessary by the use of an unfamiliar nomenclature, and by the importance given to biochemical rather than to serological reactions. The appendix that gives the technical methods for the isolation and identification of members of the *Shigella* group presupposes that the worker has available supplies of dehydrated media and commercial antisera. Other appendices deal with the control of dysentery in military establishments and in institutions.

The book contains a long and valuable bibliography in which over 2000 references are quoted.

A J H Tomlinson

NORMAN WALKER, J. N. [C.I.E. M.R.C.S (Eng.) M.R.C.P (Lond.) D.T.M. & H. (Camb.)] *Indian Village Health*. pp. iv + 90 8 plans & 2 diagrams Indian Village Welfare Association. 1944 Humphrey Milford, Oxford University Press (Indian Branch) [4s. Rs. 2-8]

This unpretentious but attractive little book has been written partly as a guide to doctors engaged on public health work, but chiefly with the aim of

of enlisting the intelligent co-operation of local authorities, voluntary organizations, and the people themselves, in improving health conditions in Indian villages. The author has exceptional qualifications for producing such a book. After a distinguished career in the regular lines of activity of an officer of the Indian Medical Service, he was selected for the important work of reorganizing the medical and health departments of the great State, Hyderabad, in South India, and for a number of years he carried out this task with conspicuous success. He writes, therefore, in the light of practical experience of the problem and deals not with what might be accomplished with the help of ample funds, a highly skilled staff and an enlightened public, but with what can be done in the absence of these advantages. He has confined his attention to the diseases "amenable to general measures in which the assistance of civil authorities and village workers can be really useful, and has strictly avoided the use of technical language.

The causes and methods of control of the chief infectious diseases are dealt with in 45 pages: there is a brief chapter on personal protection against disease, one on the organization of public-health activities and another on building regulations and the construction of minor public works. In an appendix instructions are given for the control of plague. A special feature of the book is the reproduction of detailed plans of a tuberculosis clinic, an infant welfare centre, a slaughter house, a vegetable market, a meat market, a beef shop, a village well, and an "aqua privy." These plans are reproduced on a very small scale, but they will be found very helpful to officers of health and engineers who have to undertake the construction of such works without previous experience.

The present volume is a reprint of the first edition, which was published in 1943 and probably written in 1942, so that some important recent advances such as the use of DDT are not mentioned.

Although certain details of the methods recommended are open to criticism by experts, the book can be read with profit by everyone who is concerned with the health of villages in India and other tropical countries. It is to be hoped that other public-health workers in the tropics will be stimulated to produce books dealing, on similar lines, with the special conditions of the areas in which they work.

John W. D. Meyer

COCPLAND, Reginald [K.C.M.G., C.I.E., Hon.D.Litt. (Durham) etc.]  
*Livingstone's Last Journey* 271 pp. 5 maps & 2 pls. 1945. London  
Collins, 14 St. James's Place. [12s. 6d.]

Although this book is not primarily of medical interest, readers of this *Bulletin* who have followed the literature on Livingstone, or who desire a succinct account of this period of his life, will be glad to know of the existence of this most readable book. There is evidence of a vast amount of research, but the writing is so clear that scholarship does not obtrude itself, and the story holds the attention of the reader throughout.

Charles Wilcock

# TROPICAL DISEASES BULLETIN

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## A REVIEW OF REFERENCES TO THE BONE LESIONS OF YAWS \*

By C. J. HACKETT M.D. M.R.C.P. D.T.M. &amp; H.

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There are comparatively few articles whose titles strictly refer to this subject and still fewer are based upon the study of the radiographs of more than one or two cases. For purposes of discussion the relevant publications fall conveniently into two groups. The first group includes papers in which bone lesions are mentioned in lists of cases that have received various treatments or are briefly referred to in descriptions of the disease as a whole. The second group comprises papers dealing in more detail with the bone lesions and sometimes including radiographical and pathological data. Seventy-four articles will be discussed but some others that contained nothing original have been disregarded.

### *The First Group*

Of 40 papers falling into the first group, 26 mention or make of bone lesions during the *secondary* stage of the disease. In 3 papers such an association is denied but in 11 there are records of various bone lesions occurring during this stage.

HARPER (1917) Fiji, GUTIERREZ (1922) Philippines and HUNT and JOHNSON (1923) Samoa regard all bone lesions as tertiary even (GUTIERREZ) if secondary skin lesions are also present.

Of those who record bone lesions during the secondary stage LENZ (1909) East Africa, speaks of bone and joint pain and MOSS and BIGELOW (1922) Dominican Republic mention swollen and painful joints. The following types of lesions were reported by the other authors —

Periostitis RAT (1891) Leeward Islands HALLENBERGER (1916) Cameroons

ARAÚJO (1928) Brazil HERMANS (1931) Dutch East Indies TODD (1931)

Belgian Congo D'SOUZA (1933) Nicobar Islands.

Chronic Periostitis VISWALINGAM (1922) Malaya.

Osteo-periostitis ARAÚJO (1928) Brazil TAKASAKI (1932) Caroline Islands.

Proliferative osteitis HALLENBERGER (1916) Cameroons.

Nodes CHAMBERS (1938) Jamaica.

Dactylitis HALLENBERGER (1916) Cameroons VISWALINGAM (1922) Malaya

CHAMBERS (1938) Jamaica.

Arthritis HERMANS (1931) Dutch East Indies TAKASAKI (1932) Caroline Islands D'SOUZA (1933) Nicobar Islands.

Sabre-tibia HALLENBERGER (1916) Cameroons VISWALINGAM (1922) Malaya.

\* The material for this review was collected while holding a Senior Fellowship in Tropical Medicine, of the Medical Research Council, Great Britain.

The various bones were reported to be involved as follows —

Skull and clavicle each 3 times scapula, humerus ulna, radius and carpus, once each metacarpals and phalanges 5 times ribs, once sternum, twice femur and patella, each once tibia, 4 times tarsus once metatarsals twice long bones once.

The following references to tertiary bone lesions are made in the same 40 articles. Moss and BICKLOW (1922) Dominican Republic, were not sure if tertiary bone lesions were due to yaws or to syphilis. POWELL (1923) Assam, regards all descriptions of tertiary yaws lesions as mis-diagnoses for syphilis. He had seen no such yaws lesions develop among the population whom he had closely observed for ten years following the first introduction of yaws among them. ARAUJO (1928) Brazil, regards all the bone lesions he saw as secondary because secondary skin lesions were present. He had never seen gummata or ulceration due to yaws and does not accept a tertiary stage in yaws. HARLEY (1933) Liberia, does not state the stage of the disease in his cases.

Bone lesions were recorded by the following authors —

Periostitis, acute diffuse localized, generalized multiple or hypertrophic BARR (1914) Ceylon HARPER (1914) (1917) Fiji BIKINI (1915) Papua MOSS & BICKLOW (1922) Dominican Republic HUNT & JOHNSON (1923) Samoa CALLANAN (1925) Kenya RAMSAY (1925) Assam MONTIEL (1928) Cochín China LAMBERT (1929) South Pacific DEY (1930) Assam WILSON & MATTHEW (1930) Haiti FITZGERALD & DEY (1931) Assam TODD (1931) Belgian Congo HERMANS (1931) Dutch East Indies HARLEY (1933) Liberia DE LANGEN & LICHTENSTEIN (1937) Dutch East Indies MANSION BARR (1945) STRONG (1944)

Chronic periostitis RAT (1891) Loeward Islands BARR (1914) Ceylon GUTIERREZ (1922) Philippines CALLANAN (1925) Kenya MANSION BARR (1945)

Periostitis with ulceration BAERMANN (1911) Sumatra HARPER (1914) Fiji BIKINI (1915) Papua WILSON (1924) Haiti STRONG & SHATTOCK (1930) Liberia.

Periosteal nodes HOWARD (1906) Nyasaland GUTIERREZ (1922) Philippines MANSION BARR (1945) STRONG (1944)

Nodes BIKINI (1915) Papua HOWARD (1915) East Africa DEY (1930) Assam D'SOUSA (1933) Nicobar Islands.

Nodes with ulceration HOWARD (1906) Nyasaland LAMBERT (1929) South Pacific

Bone lesions with ulceration CHAMBERS (1838) Jamaica.

Ostitis, hypertrophic diffuse localized or multiple BARR (1914) Ceylon WILSON (1924) Haiti BUXTON (1928) Oceania MONTIEL (1928) Cochín China WILSON & MATTHEW (1930) Haiti HERMANS (1931) Dutch East Indies DE LANGEN & LICHTENSTEIN (1937) Dutch East Indies SERA (1938) Belgian Congo MANSION BARR (1945)

Gummata LEWIS (1909) East Africa VUWALINGAM (1922) Malaya MONTIEL (1928) Cochín China TAKASAKI (1932) Caroline Islands DE LANGEN & LICHTENSTEIN (1937) Dutch East Indies.

Gummatous periostitis BAERMANN (1911) Sumatra HERMANS (1931) Dutch East Indies.

Gummatous nodes DEY (1930) Assam.

Gummatous ostitis BAERMANN (1911) Sumatra DE LANGEN & LICHTENSTEIN (1937) Dutch East Indies

Periosteal gummata with ulceration RAT (1891) Loeward Islands HALLER BERGER (1916) Cameroons HERMANS (1931) Dutch East Indies TAKASAKI (1932) Caroline Islands DE LANGEN & LICHTENSTEIN (1937) Dutch East Indies.

Dactylitis RAT (1891) Leeward Islands CASTELLANI (1907) Ceylon LENZ (1909) East Africa BREINL (1915) Papua de BOISSIERE (1917) Fiji HARPER (1917) Fiji MOSS & BIGLOW (1922) Dominican Republic CALLANAN (1925) Kenya BURTON (1928) Oceania DEY (1930) Assam STROGO & SHATTUCK (1930) Liberia WILSON & MATHIS (1930) Haiti TODD (1931) Belgian Congo HARLEY (1933) Liberia DE LANGEN & LICHTENSTEIN (1937) Dutch East Indies SERRA (1938) Belgian Congo MANSOY BAHR (1945) STROGO (1944) MACKIE *et al* (1945)

Sabre-tibia CASTELLANI (1907) Ceylon BAHR (1914) Ceylon WILSON (1924) Haiti BURTON (1928) Oceania DEY (1930) Assam WILSON & MATHIS (1930) Haiti HERMANS (1931) Dutch East Indies TAKASAKI (1932) Caroline Islands D'SOUZA (1933) Brazil HARLEY (1933) Liberia DE LANGEN & LICHTENSTEIN (1937) Dutch East Indies SERRA (1938) Belgian Congo MANSOY BAHR (1940) STROGO (1944) MACKIE *et al* (1945)

Epiphysitis WILSON & MATHIS (1930) Haiti MANSOY BAHR (1945)

Spontaneous fracture MANSOY BAHR (1945)

The various bones were reported to be involved as follows —

Skull 11 times clavicles 10 times scapula and humerus each once ulna and radius each 12 times metacarpals and phalanges 7 times hand bones twice ribs 7 times sternum 10 times vertebrae once femur twice tibia 18 times fibula, twice metatarsals once foot bones once limb bones 7 times

The foregoing summaries may be amplified by the following notes —

BAHR (1915) Ceylon, observed hard bony nodules resulting from the subsidence of periostitis and diffuse osteitis leading to sabre-tibia and often bowing of the forearms. Apparently a rarefying process occurs in the centre of long bones leading to spontaneous fracture and mal-union. Epiphysitis of phalanges and metacarpals leading to deformity and shortening of digits was noted and one case of ulceration obviously associated with bone lesions. HARPER (1914) Fiji speaks of perichondritis of the costal cartilages the same author (1917) Fiji, records that 15 per cent of 542 tertiary cases had bone lesions and that 75 per cent of these involved the lower limb. BREINL (1915) Papua apparently reports only tertiary yaws bone lesions and would regard some of them as a separate disease. Illustrations depict absorption of phalanges and ulceration of legs probably related to bone lesions. HOWARD (1915) East Africa reports that in children stunting or overgrowth of the ulna may lead to dislocation of the hand. GUTIERREZ (1922) Philippines found sub-periosteal nodes which altered the size and shape of the bone. periostitis was present in over 40 per cent of cases of tertiary yaws. WILSON (1924) Haiti saw the femur affected only once and thought the humerus ribs and vertebrae were exempt.

BURTON (1928) Samoa, observed ulceration with osteitis. He regarded bone lesions as tertiary for he saw few cases of primary or secondary yaws since recent systematic mass treatment had been moderately effective. MONTEL (1928) Cochun China observed ossifying periostitis with eburnation, but more often he found such destructive processes as osteo-chondritis osteoporosis with rarefaction of osseous trabeculae or rarefying osteitis. purely localized gummatous forms led to bony destruction and punched-out perforations of bones which were well seen in radiographs. He thought tertiary yaws lesions less frequent and more benign than tertiary syphilitic lesions. LAMBERT (1929) South Pacific, says that if periosteal nodes occur near the middle of a bone they cause bending. If at the ends in young people they lead to lengthening of the bone. Necrosis of bone is in his experience rare. In 1423 cases WILSON and MATHIS (1930) Haiti found rheumatic pain in 48.8 per cent. painful swollen joints in 4.7 per cent. periostitis and osteitis in 4.7 per cent. dactylitis in 0.5 per cent. sabre-tibia in 0.4 per cent.

DEY (1930) reported deformity of fingers and shortening of phalanges. STONE and SHATTUCK (1930) Liberia report dactylitis with or without ulceration and bony destruction. TOND (1931) Belgian Congo says that the periostitis of the secondary stage may accompany or precede the generalized skin eruption. TAKABAKI (1932) Caroline Islands, speaks of diffuse or circumscribed thickenings of the tibia and other bones, immediately beneath the skin. HARLEY (1933) Liberia, found bone lesions in 28 per cent. and rheumatic pain in 56 per cent. of 5,597 yaws cases; he also observed bowing of the forearm bones. He concludes that there are apparently two types of advanced active yaws: one characterized by ulceration of the skin and soft parts and the other by rheumatic pain and involvement of the bones. DE LANGEN and LICHTENSTEIN (1937) Dutch East Indies, speak of a diffuse osteitis and periostitis especially of the tibia, leading to thickening and bowing and thus to sabre tibia. SERRA (1938) Belgian Congo says that tertiary yaws bone lesions resemble those of syphilis and that the general health is usually good. He also noted irregular thickening of the tibia and hypertrophy of the femoral condyles. Parts exposed to frequent injuries were most often affected. FOX (1944) speaks of osteoperiostitis of the long bones especially the tibia, ulna, fingers and clavicle and synovitis and tenosynovitis as occurring in the tertiary stage. He does not mention secondary bone lesions.

#### *The Second Group*

The 34 remaining articles to be discussed deal with the bone lesions of yaws in more detail, and many of them are based on some radiological or pathological data. With one or two exceptions they will be dealt with in chronological order.

SCHUFFNER (1907) Sumatra speaks of bone and joint pains worse at night which were sometimes marked in the first six months of the disease; adults suffered more than children. Although these pains were present in 20 per cent. of cases he found no radiographical changes. They occurred in the first eruption or during relapses but later in the disease they were less evident. They could not be differentiated from the pains of syphilis except that they were more severe and frequent. Mercury was most effective in their treatment. He found thickening of the bones of the extremities without spontaneous pain in 4 of 63 adults and in 13 of 66 children under 14 years of age; all these 13 had the typical generalized yaws skin eruption. He reports periostitis of the middle and index fingers, fifth metatarsal, ulna and fibula causing swelling of the part. He found no rarefaction of bone tissue although his illustrations show rarefied foci in the periosteal deposits. On healing the affected bones returned to normal. He claims that the periostitis is like that of syphilis but that its localization to only part of a long bone, the absence of pain, and its onset in children allow of certain differentiation. These changes are not related to gummata of bones and respond well to mercury.

BAERMANN and SCHUFFNER (1912) Dutch East Indies regard the periostitis of the early stage of yaws as characteristic and especially frequent in children. They point out that even in the early stage of the disease lesions are not confined to the skin. In the tertiary stage there may be enormous osteitic and periostitic thickening of the tibia and bone lesions with gummatous-cystic formation.

A paper by MALL (1918) Philippines, is frequently and uncritically quoted. He describes 10 out of 20 cases with bone lesions found in 100 cases of yaws. The initial diagnosis of bone lesions in these cases was apparently based upon the complaint of pain. His publishes illustrations of only 4 of the cases. The radiographs reproduced of his "type" case are poor and suggest periosteal deposits along the radius and ulna which are not in his descriptions. Secondary

yaws skin lesions were present only in his type case a woman aged 27 with yaws of 5 months duration in the other three cases the skin lesions had healed 9 months to 5 years previously One of these patients aged 15 had contractures and large ulcers and the radiographs resemble what other writers would describe as early gummata. In another patient aged 15 he illustrates small areas of rarefaction in the articular surface of the tibial epiphysis and cortical thickening periosteal deposits and small cortical rarefied foci of the phalanges with some destruction. In the fourth case there was one small cortical rarefied focus in the calcaneum. The illustrations of Maul's type case show well-defined large oval foci up to 2-3 cm in length of cortical rarefaction in and on the surface of the cortex of the radius and ulna with probably little or no periosteal reaction Maul says that most of the lesions appear to originate in the interior of the bone but this cannot be determined from the illustrations In the hand bones are shown small cortical rarefied foci and some periosteal deposits which apparently resolved with treatment. The nodular lesions which he reports in 2 per cent. of cases and the chronic lesions which he says differ from the earlier ones are not mentioned in his case notes His illustration of chronic bone lesions with deformity is probably of lesions of tertiary yaws but he gives no details of the case He differentiates yaws bone lesions (excluding the 2 per cent. nodular ones) from syphilitic by the absence of both periosteal proliferation and cortical thickening in the former In the nodular lesions the thickening remains localized and sooner or later shows central rarefactions thus becoming the periosteal gummata of other authors. In Maul's 20 cases the frequency of involvement of bones was as follows—tibia 8 fibula 7 calcaneum and phalanges of hands and feet each 6 metacarpals and radius each 4 humerus and patella each 3 ulna femur and tarsus each 2 carpus ribs scapula, sternum and pelvis each once Lesions of vertebrae and clavicle were not observed. He concludes that in his series the joint pains were due in the most part to the presence of lesions of the articular surfaces although of his 20 cases 7 had only 2 lesions and 5 only 1 lesion in the whole skeleton. He concludes that regeneration of the bone is complete at the site of the lesion if the destruction has not been too great.

FERNANDEZ (1917) Philippines at the meeting when MAUL (1918) read his paper showed a radiograph of yaws lesions of the vertebrae but no illustration is published.

VAN NITSEN (1920) Northern Rhodesia says that osteocopic pains occur in the secondary and tertiary stages Of 699 yaws cases 459 had tertiary yaws lesions among which the following bone lesions were observed osteitis and periostitis including thickened long bones sabre-tibiae exostoses and dactylitis (77) bony necrosis from extension of yaws ulcers (27) bony rarefaction and absorption of phalanges (3) Van Nitsen does not mention gummatous lesions although his cases of bony necrosis were probably of this nature He says that tertiary lesions may occur at any age even in infants of 18 months and that the tertiary period starts towards the end of the secondary stage either with a relapse of the eruption or 10-30 years after the secondary lesions have healed.

CLAPIER (1921) French Equatorial Africa reports that the hypertrophic osteitis of yaws appears in children when the secondary rash has been generalized for some months often when it is subsiding but some typical yaws are usually still present The principal lesions are (1) goundou (2) osteitis of the short bones e.g. scapula trapezium scaphoid, etc (3) osteitis of the epiphyses of long bones (4) osteitis of the diaphysis of long bones with changes in length thickness and form which may be either localized or generalized (sabre-tibia) The phalanges are often swollen. These changes are rarely single are usually bilateral and are always accompanied by simple muscular



atrophy. In the Oubangui Clavier found that in 10 per cent. of 600 yaws cases there were bone lesions. These became less marked as the bony system developed, but permanent deformities resulted in half the cases. He rules out rickets and congenital syphilis as causative factors. He regards yaws osteitis as a tertiary lesion which nearly always encroaches on or prolongs the secondary stage.

SPITTEL (1923) Ceylon describes periosteal nodes and bony tenderness in the secondary stage but says they belong more appropriately to the tertiary period. As tertiary bone lesions he describes localized gummata or nodes which may ulcerate and diffuse periostitis and osteitis leading to osteosclerosis with bowing and deformity of long bones (sabre-tibia). Central gummata of the phalanges and absorption of these bones with shortening and ankylosis may also occur. No bone is exempt, but sites of muscular attachments are particularly affected. SPITTEL found the vertebrae involved in one case.

GUERRERO FERNANDEZ and ROSAL (1924) Philippines describe the case of a girl aged 13 who had had yaws for 6 months. The radiographs showed cortical thickening and small foci of cortical rarefaction in the proximal phalanges and metacarpals which healed under treatment with sodium-potassium tartrate-bismuthate.

MAYER (1924) quotes SCHIFFNER's description of the early bone lesions of yaws and says that the later lesions consist of large osteitic and periostitic thickenings of the tibia with deformity and also bony craters with gummatous cystic changes.

PLEEN and MEYER (1924) state that painful periostitic rarefactions sometimes combined with proliferating osteitis occur in the secondary stage. In the tertiary stage gummata on the sternum near the clavicle are characteristic. Periostitis and osteitis sometimes with gummatous ulceration of the soft tissues are also seen and in children may lead to gross deformity.

BOTREAU-ROUSSEL and CORNÉL (1924) describe the histopathological changes in specimens of goundou. These consisted of thickening of the periosteum and hypertrophy of the spongy tissue with increased trabeculae. There were also fibrous and perivascular plasma-cell collections in the spongy tissue. These were comparable with certain syphilitic changes and indicate that in yaws as in syphilis, the bone marrow is particularly liable to attack.

BOTREAU-ROUSSEL (1925) Ivory Coast, found that 75 per cent. of 130 cases of yaws osteitis occurred during or soon after the generalized skin eruption. Of these 130 cases, goundou was present in 121 and the tibia was involved 89 times, the fibula femur radius ulna clavicle humerus and phalanges were involved one to five times each. He describes cases of goundou with thickening of phalanges and long bones and the development of sabre-tibiae during or soon after the yaws eruption. In this group of 130 cases the bone lesions appeared while the secondary eruption was present in 49 per cent. (64) and soon after the eruption had healed in 33 per cent. (43). He regards these as tertiary lesions occurring during the secondary stage (see his Fig. 1). In the long bones hypertrophic osteitis was present. The periosteum was thick and adherent to the bone, the surface of which was very rough and irregular owing to the enormous dilatation of the Haversian canals whose external openings were up to 2 mm. in diameter giving the bone a spongy appearance. The medullary canal of a sabre-tibia on section was completely filled with irregularly alveolar tissue, transversely the bone was circular. Anterior bowing of the femora was also seen.

SORTOMO and EICHHORN (1925) Dutch East Indies say that except for periostitis most of the bone lesions of yaws are tertiary and resemble those of tertiary syphilis in the symmetry of their occurrence and in the sites of predilection—e.g. the occurrence of gummata in the tibia, forearm bones and cranium.

They point out that there is a fairly constant bony rarefaction surrounding the yaws lesion so that often there is gummatous softening with hyperostosis and sclerosis surrounded by atrophic changes. The bony rarefaction is apparently connected with neurotrophic disturbances and the resulting diminished rigidity probably leads to the deformities so often seen in *framboesia* particularly in growing bones. The atrophy remains for some time after the healing of the yaws process. There is no bony atrophy in syphilis. Gummatous osteomyelitis a rarity in syphilis is not infrequent in yaws and the cortex and periosteum show little reaction so that spontaneous fractures or total necrosis may occur. The final diagnosis of tertiary yaws bone lesions may depend on the history, symptoms and locality. The Wassermann reaction is usually strongly positive and is rarely changed by treatment with salvarsan and mercury. The illustrations to this paper show large foci of rarefaction with localized periosteal deposits, sabre-tibia, a spontaneous fracture, indefinite cortical rarefied foci in phalanges, calcaneal changes and total necrosis of the humerus following gummata.

KNAGGS (1926) states that in yaws as in syphilis the bones are affected in the tertiary stage. He quotes MAUL (1918) and says that Maul's illustrations do not resemble syphilitic lesions. He describes a tibia from New Guinea (in the Royal College of Surgeons Museum, England) which he compares with the lesions Maul describes and he suggests that the lesions present were probably associated with ulceration. The pitted condition he regards as quite different from the usual appearances of syphilis of long bones. Other authorities would regard these lesions as multiple gummata.

HASHIKUCHI (1927) describes the cases of 5 children who had yaws two or more years previously and were incompletely cured. They all had positive Wassermann reactions even after the bone lesions had cleared up under treatment. All had dactylitis and in 4 cases the long bones were affected. The terminal phalanges of the hands and the middle and terminal phalanges of the feet were not affected. One patient had slight nocturnal pain. Histo-pathological changes in material from the biopsy of one phalanx are reported. The periosteum was thickened and oedematous with slight diffuse cellular infiltration of lymphocytes, plasma cells, fibroblasts and polymorphonuclear leucocytes near dilated small veins (sic). Indeterminate vascular changes were present. No necrotic or cicatricial changes and no spirochaetes were seen.

POLAK (1927) Java says that the bony changes of yaws occur chiefly in the tertiary stage but they may appear early even in children, and their differentiation from congenital syphilis is difficult. Periostitis and osteitis are the most frequent changes. Long and short tubular bones may be affected, but the tibia is most frequently attacked often resulting in sabre-tibia. He describes the case of a boy aged 15 who had yaws in infancy and when seen had tendon contractures, ankyloses, tertiary ulcers, osteomyelitic foci with ulceration and spontaneous fractures and sabre tibiae. The Wassermann reaction was positive and the active lesions responded quickly to neosalvarsan. He found that the X-ray pictures resembled those of tertiary syphilis. Symmetrical gummatous processes were found in the tibia, ulna and radius and the carpal and tarsal bones; the bones of the fingers and toes were also affected. In favour of yaws was the severe bony rarefaction, gummatous and atrophic and the scanty cortical and periosteal proliferation. Cachexia is less frequent and the viscera are very rarely attacked in yaws. The history and clinical findings assist in the diagnosis of yaws.

SCHOEHL (1928) Philippines writes it is an open question whether or not the bone lesions in yaws, either early or late, are always due to actual localization of *Treponema pertenue* in the bones or whether it is a process analogous to that of keratoderma plantare which, he found occurred in monkeys in a

state of partial immunity. He says that bone lesions should be classified by themselves since they are either early or late hypertrophic, atrophic or necrotic, and may affect the periosteum or bone. In a private communication (1935) he says that in nearly 500 monkeys experimentally infected with yaws he found bone lesions developed only as an extension from skin lesions.

FOX (1929) Haiti, speaks of unilateral osteo-periostitis with fungating cutaneous gummata of the leg indistinguishable from those due to syphilis. He illustrates an inactive lesion consisting of a dense localized cortical thickening on the anterior surface of a bowed tibia.

HASSELMANN (1931) Philippines, who had worked with SCHOTTEL, says rarefying osteitis and periostitis although claimed by clinical observers as an early manifestation of yaws have never been observed in experimental infections in man or monkeys. Neither pathological changes typical of yaws nor *Treponema pertenue* have been found and it has yet to be proved that the bone lesions are not an extension of a previously healed skin lesion.

MONTÉL and COUPUT (1932) Indo-China do not mention bone lesions during the secondary stage. They found osteo-periostitis in 10-20 per cent. of cases of tertiary yaws. It was most frequent in children and adolescents and in conditions of malnutrition. It appeared 3-6 years after the secondary eruption. The limb bones were usually affected, but the ribs clavicles and all other bones might be involved. Clinically these authors recognize two forms—(1) localized nodular lesions with gumma like "gêodes" (2) diffuse osteitis, due either to extension of the nodular lesions into the cavity of the bone or to the original involvement of the cavity which leads to destruction of the periosteum, to hypertrophy or more often to rarefaction of the cortex and trabeculae and also to osteoporosis. Ulceration, they say may occur in both types. The lesions develop slowly without marked general symptoms except profound osteocopic pain but cachexia may result. Arthritis, ankylosis and sabre-tibia may occur. Response to neocarsphenamine is good. Differentiation from syphilis is assisted by the presence of yaws in the community and by the history of the patient. Syphilitic bone lesions are probably never so generalized as yaws bone lesions and in the latter the periosteal proliferation and cortical thickening so characteristic of syphilis are lacking. In 30 years in Cochin China Montel and Couput saw only one case of gonorrhea and in Indo-China where yaws is prevalent they saw none. They note the resemblance between the limb bone lesions described by BOTREAU ROUSSEL (1925) and those they have seen in yaws cases. They suggest that gonorrhea is a special aspect of African yaws and gangosa of Philippine and Malayan yaws. The illustrations show large foci of cortical rarefaction either isolated or in groups with bony expansion and some periosteal deposition. In the phalanges are small foci with cortical thickening. The osteoporosis and trabecular changes are not well shown.

BEITZKE (1934) says that differentiation of yaws from syphilitic bone lesions is difficult. In yaws osteoporosis is usually present and periostitis is found during the secondary stage. Tertiary bone lesions may occur early even while secondary skin lesions are still present. They are periosteal and osteomyelitic gummata, which are usually localized, though numerous foci may exist in one bone. These lesions produce only slight bone formation. Spontaneous fractures are more frequent than in syphilis and callus formation is slight. Periosteal and cortical gummata frequently ulcerate. The same bones are affected as in syphilis the skull and tibia most frequently but also the phalanges metacarpals metatarsals ulna and fibula. In the tibia, hyperostoses with sabre-tibia also occur. Sabre-tibia is more frequent in yaws than in syphilis. Contractures and ankyloses are also found.

MONTEL, MASSARI and LE VAN PHUNG (1934) Annam describe the case of a boy aged 15 who had yaws 9 years previously with bone lesions of several years duration. The affected parts were swollen and on the legs gummatous ulceration extended to the bone. Two types of lesion were seen in the radiographs (1) localized diaphyseal thickenings with condensation of the periosteum and deep tissue encircling the bone or on one side only and (2) *géodes* [gummata] of various sizes but always round and well-defined in these thickenings and associated with further marked condensation. Between these last lesions there might be slight decalcification. The authors say that the number of the *géodes* the irregularity of the hyperostoses and the narrowing of the medullary canal, differentiate these yaws lesions from those of syphilis. The illustrations are good and show expansion cortical thickening and large foci of cortical rarefaction in the bones of the forearm.

WOLTER (1934) concludes from the absence of spirochaetes in them that the lesions of the phalanges in yaws are an allergic reaction to the organism. He also suggests that the absence of spirochaetes in these lesions may be due to framboesial spores such as have been assumed in syphilis but he admits that this does not account for the predilection for the phalanges.

The *Jamaica Yaws Commission Report* for 1936 states that there are probably some bone lesions in the majority of cases of yaws in the early stages with pain and tenderness. Perhaps 15 per cent. of yaws cases have bony swelling and tenderness. The long bones especially of the forearm and leg are most frequently affected but the skull phalanges or any other bone may be involved. Bone changes are perhaps most frequent during the secondary stage but they also occur later and may be associated with ulceration. The course of localized swelling fluctuation and ulceration has been observed. Great deformity frequently results and also bowing of the legs and forearms. The radiographical appearances are fairly constant and often characteristic (1) widespread multiple areas of rarefaction with or without surrounding increased density and (2) fusiform enlargement due to periostitis causing thickening of the cortex or (3) great enlargement with sclerosis of cortex and medulla. The Report for 1932 states that no spirochaetes were found in material collected from bone lesions.

HACKETT (1936) Australia traces part of the development of sabre tibia and describes certain other lesions found in aboriginal bones which he suggests are due to yaws. No account was taken of the stages of the disease in which the lesions occurred. Secondary skin lesions were rarely seen. All the lesions that were suggested to be of yaws origin have been described by observers in yaws communities.

MACKAY (1938) criticizes the suggestion of HACKETT (1936) that certain lesions in aboriginal bones are due to yaws. He describes and illustrates a number of the 350 specimens he examined in the Australian Institute of Anatomy Canberra and divides the bony changes he observed into periostitis osteitis with rarefaction and sclerosis and osteomyelitis. He concludes that they result from venereal syphilis an endemic type of non venereal syphilis or some unknown indigenous disease. He regards venereal syphilis as the most probable. [Excluding the fractures and joint and skull changes many other lesions strikingly resemble the bone lesions of yaws reported in yaws communities and observed by Hackett in Uganda. MACKAY's exclusion of yaws as a possible cause is based upon published accounts of disease in Australian aborigines without apparently any observations or enquiries by himself concerning the diseases at present occurring in isolated aboriginal communities. The only articles on yaws bone lesions to which he refers are SPITTEL (1923) KNAGGS (1926) and P. MANSON *Tropical Diseases* (no date).]

BOTREAU ROUSSEL, FRAGES and GAUTHIER VILLARS (1937) Ivory Coast, describe the histopathology of yaws bone lesions in specimens from 20 biopsies. The main changes were thickening of the periosteum, in which were small collections of lymphocytes and plasma cells. They also observed vascular sclerosis decalcification lamunar absorption and osteoclasts. There were increased fibrous tissue and plasma cell infiltration in the medullary spaces. Giant cells, marked bony destruction and spirochaetes were not found. These authors could not describe any changes as characteristic.

BOTREAU-ROUSSEL (1937) Ivory Coast regards all the bone lesions of yaws as secondary lesions. Pain is present in most cases of secondary yaws at some time. Clinically there is no difference between the bone lesions (osteopenostitis) at the onset and the deformities found years later. He never saw necrotic excavated lesions or gummatous nodules with ulceration such as those described by MONTIEL in Indo-China. The onset, he says, may be abrupt or gradual with swelling over the bone tenderness and increase of the pain which is worse at night. General symptoms may be absent. Over 40 per cent. of 75 cases under 2 years of age had obvious bone lesions. In 130 cases the following bones were affected—phalanges, 36 per cent. metacarpals and ulna each 15 per cent. tibia 14 per cent. radius 12 per cent. fibula, 5.5 per cent. femur humerus and others each 0.5 per cent. skull, 0.2 per cent. foot bones and goundoun each 0.15 per cent. BOTREAU ROUSSEL states that fingers may be swollen and turgid, the long bones thickened or fusiform and, in advanced cases deformed by exaggeration of normal curves or by exostoses. Severe pain may last months or years but osteitis may continue after pain has ceased. In the hand, joints may be involved and spontaneous fractures occur with resulting deformity. Ankyloses mal-union of spontaneous fractures and sabre-tibia may result. Diffuse or localized swellings of the skull are found. Soft tissue changes resolve and leave the bony thickenings more obvious. The histopathological changes are those he described earlier (1924 and 1937). In early cases the periosteum is thickened and the bone soft the bone is spongy from dilatation of the Haversian canals which, in marked cases are filled with fibrous tissue. In old cases the cortex is dense and hard. In radiographs the periosteum is seen to be loosened and separated by inflammatory tissue this phase is soon followed by thickening of the underlying cortex and reaction of the medullary tissue so that fusiform thickening of the bone and narrowing of the medulla result. In advanced lesions the Haversian canals considerably enlarged by fibrous tissue give the swollen bones the lacunar appearance of fibrous osteitis. Later there is organization and bone is deposited round the enlarged Haversian canals. This author discards the suggestion that poor resistance or malnutrition plays an essential part in the production of bone lesions. His illustrations show sabre-tibia periosteal deposits expansion and cortical thickening and small foci of cortical rarefaction which he attributes to dilated Haversian canals.

CARRON (1937) French Colonies, says the transition from the secondary to the tertiary stages is more theoretical than real. During the secondary stage rheumatic joint and osteocopic pains periostitis and dactylitis occur and in the tertiary osteopenostitis, bony deformity contractures and ankylosis. These tertiary lesions may appear while the secondary lesions are still present, but more often they develop 2-6 years after infection or even after a latent period of 30 years. It is difficult to differentiate tertiary yaws from syphilitic lesions and figures for their incidence are of doubtful value as there is so often confusion. Carron refers to MONTIEL, COURTOY and BOTREAU ROUSSEL for descriptions of yaws bone lesions. The incidence of tertiary yaws lesions is higher where the incidence of yaws is highest hence he is prepared to consider a tertiary stage in yaws and not to regard these lesions as syphilitic as he did until recently.

SIMPSON (1938) *Cameroons* does not mention bone lesions during secondary yaws. Tertiary bone lesions commence five or more years after the secondary stage. The onset is indicated by pain and a small tender swelling. Radiographs show the periosteum raised from the cortex. This process extends along the bone. Decalcification of the underlying cortex follows causing a moth-eaten appearance and calcification of the periosteal changes takes place finally diminished vascular supply leads to bony sclerosis. Ankylosis and ulceration may occur. The apparent bending of the tibia according to this author is due to periosteal deposits on the anterior surface and not to deformity of the long axis of the shaft. There were no cases of sabre-tibia in 920 cases of yaws seen by himself nor in the 30 000 yaws cases dealt with by 80 African yaws attendants. He suggests that some diietetic deficiency is the cause of this deformity. He says the whole of the pathology of yaws is confined to the surface of the body the skin and superficial bones being the chief sites of the lesions e.g. the leg forearm and clavicle. Post mortem examination of 20 cases of suspected yaws showed osteitis with varying degrees of rarefaction and sclerosis of bone. His illustrations which are poor show periosteal deposits cortical thickening and expansion and cortical rarefaction and periosteal deposits.

BRYANT and FAIRMAN (1939) Sudan say that bone lesions in yaws are common in Nilotics (Dinka Shilluk and Nuer) and uncommon in forest dwellers (Azanda Bongo and others).

WILLIAMS (1939) in a recent text book of X ray diagnosis quotes only from MAUL (1918) KNAGGS (1926) and WILSON and MATHIS (1930) and repeats the confusion of comparing the New Guinea tibia (R.C.S. England) with the changes described by MAUL.

GOLDMANN and SMITH (1943) from a study of 101 cases in African soldiers and civilians at Sierra Leone stress the difficulties of differential diagnosis.

Diagnosis of yaws was based upon the presence of typical yaws scars quick response to treatment and the positive Kahn reaction. The following frequency of bone involvement was observed the tibia in 46 cases fibula in 20 femur in 13 ulna in 10 humerus in 9 radius in 7 and other bones each in less than 5. The authors illustrate a vertebral lesion and report skull lesions and spontaneous fractures. Gummata were noted especially in the ribs clavicle and pelvis. Trauma was considered an important factor in imitating lesions. During active growth joints and epiphyses are attacked.

The first sign of activity is said to occur in the cortex and resembles the lesions described by MAUL (1918) or are of more moth-eaten appearance. The later stages they regard as either heavy thickened bones or shrunken bent ones.

They believe the absence of periosteal deposits in the presence of cortical lesions [the bony expansion they described must have arisen from the periosteum] and the frequency of fibular lesions in yaws differentiate it from syphilis. Other lesions that might lead to confusion are osteomyelitis osteitis deformans and tuberculosis. [It is probable that the authors refer only to tertiary bone lesions they do not mention any secondary bone lesions.]

HELFET (1944) deals with acute bone lesions in West Africans mostly soldiers. In all cases the Wassermann and Kahn reactions were positive. He regards trauma as often initiating the lesions which soon develop marked changes. Acute onset with rheumatic pain and fever was frequent. The tibia femur clavicle and humerus were most frequently affected, but vertebral and skull lesions occurred. Joints and tendon sheaths were also involved. He says that yaws bone lesions are more rapid in development and are more painful than syphilitic ones.

X-ray appearances were increased diameter and density of bones or multiple layered periosteal deposits over diffuse cortical rarefactions. Microscopically

the bone lesions resembled syphilitic lesions except for the absence of endarteritis [In this paper too probably only tertiary lesions are described.]

ASH and SPITZ (1945) regard bone lesions as tertiary. They say the tibia is most frequently involved and the early lesions are small foci of cortical rarefaction which lead to a diffuse worm-eaten appearance of the entire shaft. The resulting weakening of the bone leads to sabre-tibia. They speak of the development of "marble bones" in which fracture easily occurs. Gummata may occur in flat bones but are seldom in long bones. In children epiphyses and joints may be affected. The absence of periostitis in the presence of osteoporosis in yaws differentiates it from syphilis. They include gonorrhea and gangosa in the tertiary stage [Their illustrations of lesions of the hand bones are almost certainly secondary not tertiary]

#### SUMMARY

The 70 articles dealt with above although not including every reference to the bone lesions of yaws are representative of the literature of this subject. The first point that comes to notice is the absence of any complete radiological study of these lesions. French and Dutch authors have added most to the knowledge of the subject since the earlier work of SCHUFFNER (1907) and MAUL (1918).

Many of the differences in the various descriptions are probably due to the incompleteness of the studies upon which they are based, but it is remarkable that BOTTEAU-ROUSSEL (1937) Ivory Coast, saw no destructive bone lesions comparable with those described by MONTEL *et al.* (1932 and 1934) Indo-China. SOETOMO and EICHHORN (1925) and POLAK (1927) Dutch East Indies, HACKETT (1936) Australia, and by others in other parts of the tropics who had made no radiographs. Although these "bony gummata" were described in other parts of Africa by HOWARD (1903) Nyasaland LEWIS (1909) East Africa HALLENBERGER (1916) Cameroons and probably SIMPSON (1933) Cameroons no radiological evidence has been produced.

Another feature of the literature is the absence in many articles of any reference to bone lesions occurring during the secondary stage of yaws while some authors maintain that all bone lesions belong to this period of the disease others state that they are all tertiary lesions. Here again there is no definite geographical grouping to account for the differences found. In the series of cases studied in Uganda by the reviewer and to be reported elsewhere lesions were found in all stages of yaws and practically all the lesions described above were observed.

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## MALARIA.

CALDWELL, J. D. *Malaria Control in the Dominican Republic. Puerto Rico J Pub Health & Trop Med.* 1945 Dec v 21 No. 2, 193-200 [Spanish version 201-8.]

The Dominican Republic (Santo Domingo) occupies the eastern two-thirds of the island of Hispaniola (Haiti) lying to the east of Cuba and Jamaica in the West Indies. The climate is typical of the Caribbean region with a rainy season between May and October heaviest in the spring and autumn and totalling 100 inches per annum in some parts. Malaria is prevalent varying in intensity in different communities: spleen rates vary from 0 to 42.8 per cent. Among 1,574 positive blood smears 72.8 per cent. showed *Plasmodium falciparum* 17.18 per cent. *Plasmodium vivax* 4.73 per cent. *Plasmodium malariae* and 5.61 per cent. mixed strains. *Anopheles albimanus* is the principal malaria vector. Streams are the main breeding places, but swamps, lagoons and irrigation systems may also be involved. A Malaria Division of the Health Service was formed in 1941. In relation to certain urban areas where seasonal clinical malaria occurs permanent major and minor drainage schemes have been instituted. The author states that requisite personnel are being trained and that larvicidal control is to be commenced.

R. Ford Tredd.

BERBERIAN D A The Species of Anopheline Mosquitoes found in Syria and Lebanon. Their Habits, Distribution and Eradication. *J Palestine Arab Med Ass* 1946 July 1 No 5 120-46 1 map & 10 figs [Numerous refs]

To enable the reader to understand the problem of anophelism in Lebanon and Syria the author outlines the main topographical and climatic features of the territory. He then gives an account of the morphology, distribution and habits of the anopheline mosquitoes, comments on their importance as vectors of malaria and discusses the possibility of their eradication from the country.

Two mountain ranges run parallel to the sea coast: the western range comprises the Lebanon mountains and the eastern the Anti-Lebanon range. To the west of the Lebanon mountains is the coastal belt between the ranges is the highly cultivated Beka plain and east of the Anti-Lebanons is the Syrian desert. The Euphrates river passes through the north-eastern parts, the Orontes rises in the Beka and flows north, the Litani also rises in the Beka but flows south and the Barada flows east through Damascus. Many rivers cross the coastal strip, the majority are small, dry streams which dry up in late summer. Coastal swamps exist at the river mouths and there are a number of inland swamps and lakes. Ancient and modern irrigation canals, cisterns, wells, holes and man-made depressions are scattered all over the countryside.

The climate of the coastal belt is generally sub-tropical, that of the mountains temperate and that of the Beka extreme. From May to October heat and dryness increase from west to east and little moisture crosses the Anti-Lebanons which form a barrier between Syria and the Syrian desert. Wind is generally from the west and south-west.

The species of Anophelines are *A. sacharovi*, *A. superpictus*, *A. claviger*, *A. sergenti*, *A. hyrcanus*, *A. algeriensis*, *A. martens* and *A. multicolor*. The first seven are established north of the border. The first three are important vectors of malaria. Keys are provided for the identification of adults and larvae and a table is given of characters for the separation of the closely allied *A. claviger*, *A. algeriensis* and *A. martens*. The figures are unfortunately rather indistinctly reproduced.

*A. sacharovi* is capable of maintaining intense malaria. It breeds in inland and coastal swamps and in springs, cisterns and pools where the water surface is covered with a layer of vegetation. In winter females settle in houses, barns and stables near a food supply from whence they emerge on warm days to feed and then retire to their hiding places. *A. sacharovi* is a strong flier and in the Beka may travel five to ten kilometres aided by the wind.

*A. superpictus* transmits much of the rural malaria, particularly in the coastal belt. Larvae are commonest from May to October in the sunlit parts of mountain streams among stones and boulders, in springs, ditches and irrigation channels. They also occur in water which collects in sand and gravel pits. *A. superpictus* breeding places are flooded out in winter, consequently control measures need to be repeated each season. Adults enter houses and stables at night but their flight range is limited, possibly to a maximum of two kilometres.

In towns and villages *A. claviger* is the important species and breeds in wells though if the spleen rate is over 10 per cent. breeding places of other species may be implicated. Introduction of piped water supplies has sometimes worsened the situation because the disused wells have remained untreated. In rural areas shaded parts of rivers and mountain streams also breed *A. claviger* which is the first anopheline to appear in springtime.

The transmission of malaria in this region by *A. sergenti* is not confirmed but it must be regarded as a potentially dangerous species. Larvae are sometimes found with those of *A. superpictus* in stream beds, canals and ditches, but not in marshes. Its flight range is not great and it is thought to overwinter as an adult.

The remaining species are unimportant. *A. hyrcanus* and *A. algeriensis* breed in marshes and will bite in sunlight. *A. marleri* breeds in shaded pools in hilly country. *A. multicolor* has not established itself in Syria and Lebanon.

The author suggests that the attack on the three malaria vectors should consist in spraying winter quarters of *A. sacharovi* and *A. superpictus* with 5 per cent DDT in kerosene or 5 per cent DDT emulsion once in December or January and once in March followed by treatment (with Paris green malarial or DDT) of all potential breeding places once a fortnight. In the case of *A. claviger* he suggests that wells and cisterns be sprayed every two months in rural areas be considers that the *superpictus* control measures will suffice for the *claviger* problem also. He believes that it is possible to devise and execute such an extensive programme and proposes that advice and direction should be sought from those who dealt with the eradication of *A. gambiae* from Brazil and Egypt.

H S Leeson

KALANDADZE L P & SAGATELOVA, I S [Concerning Dry Hardiness of Mosquito Larvae on Dry and Humid Substrata.] *Moscow Parasit & Parasitic Dis.* Moscow 1945 [1946] v 14 No 6 19-25. [In Russian.]

Working with larvae of *Anopheles maculipennis maculipennis* *A. bifurcatus* [*A. claviger*] and *Culex pipiens* the authors carried out a series of experiments with the view to determining their viability on dry and humid substrata. The striking term dry hardness is used by the authors. Batches of 20 larvae of each age-group were placed in 100 cc crystallizers containing at the bottom a layer of earth sand, plants chips of wood or a filter. After exposure for different periods of time water was added to the substratum and on the following day a count was made of the percentage of live and dead larvae. In a control crystallizer water was added at the beginning of the experiment. Experiments on humid substrata were carried out with a special apparatus [see this Bulletin 1944 v 41 916.]

The results were as follows — (1) The dry hardness of mosquito larvae is considerably less than that of the eggs. (2) the dry hardness of larvae of stages I and II is less than that of larvae of stages III and IV. (3) larvae of *Culex* are more dry hard than those of *Anopheles*. (4) at lower temperatures of the air the hardness of larvae increases both on dry and humid substrata. (5) the dry hardness of larvae on humid substrata (33 per cent moisture in the soil) is considerably higher than that on perfectly dry substrata. Thus the larvae of *A. bifurcatus* of stages II, III and IV can live from 3 to 7 days on humid substrata at 23-24°C and 50-75 per cent relative humidity whereas on dry soil they survive only up to 35 minutes at 24°C.

C A Howe

FEDERATED MALAY STATES INSTITUTE FOR MEDICAL RESEARCH. The Anopheles of Malaya. Keys for the Identification of the Females and Larvae of the Anopheles Mosquitoes found in the Malay Peninsula. 48 pp. numerous illustrations. 1945 [Prepared by the Staff of the Entomological Division of the Institute for Medical Research F.M.S.]

This handy little booklet is a practical introduction to the identification of Malayan anophelines. It will be useful both to medical and non medical investigators.

The text is simple and accurate. Detailed descriptions of mosquito anatomy are not included but the important morphological features are clearly indicated in the diagrams. In thirty-seven pages the reader is shown how to recognize mosquitoes how to distinguish culicines from anophelines and the different species of *Anopheles* from one another. Instructions are given for using the keys for the identification of females and larvae of Malayan species. The keys are followed by brief descriptions of eighteen important species notes on their habits distribution breeding places and relation to malaria and a brief glossary of some technical terms.

In the few remaining pages there is a short account of malaria in the Malay peninsula and a description of the man baited double net method of trapping mosquitoes.

H S Leeson

DAGGY R H. The Biology and Seasonal Cycle of *Anopheles farauti* on Espiritu Santo New Hebrides. *Ann Ent Soc Amer* 1945 v 38 No 1 1-13  
[Summary taken from *Rev Applied Entom* Ser B 1946 Aug v 34 Pt 8 122-3]

*Anopheles farauti* Lat. \* the mosquito formerly known as *A. punctulatus moluccensis* Sw & Sn \* occurs in the New Hebrides (including the Banks Islands) the Solomons Bismarck Archipelago Admiralty Islands and eastern New Guinea and is the most important vector of malaria in the Australasian region. It was studied from October 1942 to September 1943 in Espiritu Santo (New Hebrides) where it is the only Anopheline and malaria is hyperendemic. An account is given of the precipitation geological structure and drainage of the island. *A. farauti* is primarily a coastal mosquito though the author found it to be abundant at an altitude of 1 100 ft. on Gaua Island in the Banks Group. Permanent breeding places in Espiritu Santo include rivers streams springs taro gardens seepage areas ponds lakes swamps marshes open wells and fresh water and slightly brackish lagoons. During the rainy season breeding occurs also in such temporary sites as pools ruts and hoofprints. The breeding places vary widely in respect to sunlight temperature plant growth turbidity and movement. Breeding and malaria transmission occur throughout the year wherever water is available but in the south-eastern part of the Island, where there are few permanent breeding places transmission takes place principally in the rainy season. At this time adults are produced in large numbers in all breeding places except some of the larger rivers from which the larvae are flushed by frequent floods. It is estimated that troops were responsible principally through the construction of roads and the movement of heavy equipment for the formation of 90 per cent of the temporary breeding places in the area in the south-east that has been occupied by them. Moreover the suitability of some permanent water for breeding was increased. The natives favour the transmission of malaria by building villages near rivers and by making water terraces for growing water taro a staple food crop.

The flooding of low lying fresh water marshes with sea water was considered as a possible control measure but investigation showed that the maximum salinity at which breeding can occur is high. Females given a choice of 11 dishes containing water of different salinities varying from rain water to pure sea water oviposited in almost all including the pure sea water though they seemed to have some preference for concentrations of less than 50 per cent. sea water. Eggs hatched in pure sea water but the larvae died in a few hours.

It appears from a recent key that American authorities have concluded that *A. farauti* is specifically distinct from *A. punctulatus* Dön., and that *moluccensis* H., as is probable is a distinct form is a sub-species of *farauti* and not of *punctulatus*.

However complete development took place in water containing 13 000 parts chlorides per million (65 per cent sea water) larvae were found in nature in water containing 13 500 parts chlorides per million (68 per cent sea water) and larvae taken from such water in the second or third instar completed their development in partly evaporated sea water containing 23 000 parts chlorides per million. Opening low lying areas to sea water may therefore increase the area available for breeding but where tidal flushing is marked and the water is not impounded larvae are greatly reduced in numbers or eliminated.

In individuals reared in the laboratory at 23-30°C [82-4-86°F] on dog biscuit the egg larval and pupal stages lasted 1½-2, 10 and 1½ days respectively. The cycle in open sunlit pools is probably shorter. The females attack man readily though they also fed on animals. In houses or tents with artificial light they bit chiefly in shaded corners or on shaded parts of the body. They fed principally but not exclusively at night. Their bite is painless and their flight relatively quiet. They sometimes used artificial shelters such as dwellings, tents, boxes and large tins as diurnal resting places but were also found on the walls of slit trenches and the underside of logs. They were never found, however in standard boxes placed in favourable situations in attempts to estimate adult populations. From observations on the distances between areas in which malaria occurred in the dry season and the nearest breeding places it was estimated that the effective flight-range of the females is ½-1 mile and intensive control measures within this radius considerably reduced the malaria rate. A female was found, together with mosquitos of other species on a boat 600 yards offshore where the crews of several boats were reporting mosquito annoyance at night and becoming infected with malaria.

Filaria with nocturnal periodicity is endemic in the New Hebrides. Of the mosquitos occurring there the only ones in which the complete development of *Filaria* (*Wuchereria*) *bancrofti* has been observed are *A. farauti* and *Culex fatigans* Wied (*quinquefasciatus* auct.) and as the latter is recently introduced and rare *A. farauti* is probably the important vector.

EADS, R. B. A New Record of *Anopheles albimanus* in Texas. *J. Econom. Entom.* 1946 June v 39 No 3 420

"Five *Anopheles albimanus* females were taken within a two-week period from three different locations near the Corpus Christi Naval Air Station. This represents the first known migration of this species from the Lower Rio Grande Valley into other parts of Texas.

PACKER, H. The Use of Darkfield Illumination in Studies of Malaria Parasites. *J. National Malaria Soc. Tallahassee Fla.* 1945 Dec. v 4 No 4 331-40 5 figs.

In this paper the author gives an account of his experience with the use of dark field illumination for the study of malaria parasites. He describes the apparatus he has found most useful and his method of preparing blood for examination. He advocates the admixture with the blood of a little distilled water or tap water by inserting a small drop of water on the coverglass on to the drop of blood on the slide. Rapid detection of *Plasmodium vivax* was possible owing to the brilliant refractiveness of its pigment which was in active Brownian movement. The method is less satisfactory for *P. falciparum* owing to the paucity of pigment in the young rings which are the forms in the peripheral blood. Observations are readily made on the process of exflagellation. The author concludes that when blood examinations are intended for the discovery of *P. vivax* alone the dark field method is often the most rapid for obtaining a diagnosis.

C. M. Henry

GUTH, G. S. A Case of Quinine Amblyopia. *Indian Med Gaz* 1946 June-July v 81 Nos. 6-7 238-41 5 charts.

HALAWANI A. & NOR EL DIN G. A Case of Raynaud's Disease-like Condition of Unusual Severity following Intramuscular Quinine Injections. *J Roy Egyptian Med Ass* 1946 Jan-Feb v 29 Nos 1/2 84-9 2 figs

1. A case presenting the signs and symptoms of Raynaud's syndrome was described. The patient was a female Mohamedan aged fifteen years from the Dakhla Oasis of the Egyptian Western Desert. She was suffering from chronic malaria and syphilis but there was no haemoglobinuria.

2. The point of interest of this case are the close relation between the administration of quinine in the gluteal muscles and the onset of the lesion the severity of the condition leading to gangrene with complete loss of the toes) and its occurrence in only one limb and that limb being the lower extremity.

LANGE K. & MATZNER M. J. The Distribution of Atabrine in the Blood, the Skin, and its Appendages. Methods for the Rapid and Simple Detection of the Presence of Atabrine in Blood, Skin, and Nails. *J Lab & Clin Med* 1946 July v 31 No 7 742-8 4 figs 10 refs

The authors have used a single extraction method in conjunction with a fluorocomparator to estimate plasma levels of atabrine. The earlier methods described for the estimation of this substance this *Bulletin* 1938 v 33 273 1938 v 36 103 569 lacked sensitivity while the methods of BRODIE and LUDWIG and of MASEN this *Bulletin* 1944 v 41 453 1945 v 42 87 which meet all requirements demand considerable skill and laboratory resources. The present method consisted in basifying the plasma and extracting atabrine base with ether. Fluorescence in the extract was then measured by a fluorophotometer or visual fluorocomparator with selective light filters to cut off undesired fluorescence repeated extraction with solvents was thus avoided. The technical details of the instruments are described. By the above means the plasma levels in 22 patients receiving atabrine for treatment of relapsing *P. vivax* infections were studied. The authors found that 0.3-0.6 gm. atabrine on the first day followed by 0.2 gm. daily for 7 days was not sufficient to give a desired plasma level of 100 microgrammes per litre but that this level can be reached in 24 hours if 1.2 gm. is given on the first day followed by 0.6 gm. on the following day and 0.3 gm. daily thereafter during treatment. Use was also made of ultra violet light of wave length 3600 Ångström units to excite fluorescence in the skin and appendages of atabrine treated patients which could be observed visually or measured quantitatively by a photoelectric Dermofluorometer previously described. No direct correlation was found between the amounts of atabrine present in plasma and skin. Observation of the fluorescence in nails readily indicated whether atabrine was being taken regularly. J. D. Fulton

SMITH L. H. & STOECKLE J. D. Effect of Quinacrine Hydrochloride (Atabrine) on Isolated Mammalian Heart. *Proc Soc Exper Biol & Med* 1946 June v 62, No 2 179-84 2 figs [13 refs]

A study was made of the effect of adding mepacrine to the heart lung preparation of dogs. Contractility of the heart muscle was impaired, so that the output of the heart diminished and the volume of the heart increased. The outflow from the coronary sinus did not change significantly. Bradycardia occurred sometimes but not always. The electrocardiograph was approximately normal. These changes could be reversed by adding cardiac glucosides.

(ouabain or K-strophosid) The minimal toxic concentration of mepacrine was about 1 mgm. per litre of whole blood 1.5 mgm. per litre was regularly toxic Much of the mepacrine was rapidly removed from the circulating blood 50 per cent disappeared from the blood in 15 minutes in one experiment in another 90 per cent disappeared in about 50 minutes although the heart and lungs are the only tissues available in the preparation to take it up Rapid injection of mepacrine leads to severe heart failure but a slow infusion of the same amount can readily be tolerated Accordingly if mepacrine is to be given intravenously it should be given extremely slowly *F Hawking*

GUTIERREZ SÁNCHEZ Elena Acumulación y excreción de la atebriina en el ratón [Concentration and Excretion of Atebrin in Mice.] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico 1946 Mar v 7 No 1 1-12, 1 graph 14 refs Summary in English by the author

A study was made of the concentration of atabrine chloride, *sic* in the original it is Clorhidrato in the blood of white mice its excretion in the faeces and urine and its storage in the liver spleen lungs heart intestine and kidneys. The drug was administered orally 113 mgs per kilogram of weight 24 mgs. intravenously and 25 mgs intraperitoneally in a single dose and repeated doses

"The atabrine concentration in the blood with one daily dose for several days never exceeded 0.50 mgs per cent but this low concentration continued for five days after treatment was suspended.

High concentrations of the drug were found in the liver disappearing completely eight days after the treatment was suspended Lower concentrations were found in the spleen and lungs

BARFORD F R CURD F H S & ROSE, F L Synthetic Antimalarials. Part VIII. Some 4-Arylamino-6-Aminoalkylamino-2-Methylpyrimidines. *J Chem. Soc* 1946 Aug 713-20

CURD F H S DAVIS, M I OWEN E C ROSE, F L & TURY G A P Synthetic Antimalarials. Part IX. 4-Arylamino-2-Aminoalkylamino-6-Methylpyrimidines. Further Variations. *J Chem Soc* 1946 Aug 720-29

CURD F H S & ROSE, F L Synthetic Antimalarials. Part X. Some Aryl-Diguanides ("Bisguanides") Derivatives. *J Chem Soc* 1946, Aug 729-37

KAPLAN L I READ H S & BECHER F T The Action of Thiobismol on Therapeutic Quartan Malaria. *J Lab & Clin Med* 1946 July v 31 No 7 733-41 1 fig

It was shown by SCHWARTZ (*J Pharm. & Exper Therap* 1939 v 65 175) that sodium bismuth thioglycollate (thiobismol BI ( $\text{SCH}_2\text{COO}\backslash\text{a}$ )<sub>2</sub>) had some effect in controlling the number of paroxysms during therapeutic malaria treatment with *P. malar.* LOTAG *et al* [this *Bulletin* 1943 v 40 881] failed to obtain consistent results with *P. malariae* and the drug was apparently without action on *P. falciparum*. Investigation has now been made with this drug in 38 patients with blood induced *P. malariae* infections who were experiencing true quartan double quartan or quotidian attacks in order to find out at what stage of growth the parasites are affected and also its effect on the paroxysms. Fifty-six injections of the drug in 0.1 or 0.2 gm doses were given intramuscularly at irregular intervals. Its controlling effect on the paroxysms was decided by relating the time of administration to the growth stage of the parasite in all types of cycle encountered. Young or mature forms of the parasite were

practically unaffected. In about half the patients with true quartan cycles the drug exerted a definite clinical effect because of its action on immature forms of the parasite. Paroxysms were interrupted in a very large percentage of patients experiencing the other types of cycle and the partially mature forms of the parasite were chiefly affected. Patients with parasite counts above 10 000 per cmm. showed no clinical response to treatment but the parasite numbers were reduced. The authors conclude that in quartan malaria the drug is of value in reducing the frequency of paroxysms and in controlling irregular cycles. It should aid neurosyphilitics undergoing treatment to tolerate better a full course of therapy with this parasite.

J. D. Fulton

CLUVER F. W. P. Report on Malaria Control in Rural Native Areas by using D.D.T. Insecticide. *South African Med J* 1946 July 13 & 20 No. 13 368-70

The author working in a Zululand Reserve reports on the substitution of weekly insecticidal spraying of native huts with Pyagra paraffin by the alternative method of 5 per cent DDT in commercial paraffin. The local anopheline vectors of malaria are *Anopheles gambiae* and *A. funestus*. The results in an admittedly small scale experiment illustrate the inefficiency of a weekly pyrethrum spraying programme when compared with the degree of adult mosquito eradication attained with DDT.

Park Ross instituted insecticidal spraying in Zululand this *Bulletin* 1937 & 34 581 with resultant control of seasonal epidemic malaria. It remains to be seen what effect the general use of residual DDT as described by the author will have on endemic malaria.

The author quotes a saving of 12 per cent in costs in the replacement of weekly Pyagra by three-monthly residual DDT. The additional benefit of a heavy fly and cockroach mortality is noted.

R. Ford Tredre

JOHNSON H. A. & EASON J. L. Jr. DDT in Paradichlorobenzene as a Larvicide. *Pub Health Rep* Wash. 1946 Aug 9 & 61 No. 32, 1185-8 1 fig

DDT pellets were prepared by melting paradichlorobenzene and adding solvents containing DDT and emulsifiers and DDT in crystalline form. Details of two of the seven formulae are given here as examples —

- { 475 cc. paradichlorobenzene
- 25 cc. of a 50% solution of DDT in Velsicol 70 plus 1.5% Triton X 100
- 20 gm. DDT
- { 475 cc. paradichlorobenzene
- 25 cc. of a 7% solution of DDT in No. 10 motor oil.
- 20 gm. DDT

Suspension of the pellets in water in field experiments resulted in slow disintegration 50 per cent of volume in 14 weeks. A marked reduction in mosquito larvae occurred for the first six weeks after which scum and vegetation began to interfere with the action of the DDT. The authors consider the results attained were promising and that a higher rate of pellet disintegration would result in a higher degree of *Anopheles* control.

R. Ford Tredre

KRUSE C. W. & METCALF R. L. An Analysis of the Design and Performance of Airplane Exhaust Generators for the Production of DDT Aerosols for the Control of *Anopheles quadrimaculatus*. *Pub Health Rep* Wash. 1946 Aug 9 & 61 No. 32, 1171-84 5 figs.

The authors describe a method of control from the air by DDT larvicide of the larvae of *A. quadrimaculatus* under conditions encountered on the unpounded



waters of the Tennessee Valley Authority. Spraying of such areas is attained by the atomization of a DDT solution by the exhaust gases of the airplane engine. The larvicide is injected into a venturi extension of the engine-exhaust by a wind-driven pumping unit. The following desirable factors in a DDT solvent for this use are quoted —

(1) High solvent power to permit the use of concentrated solutions which greatly increase payload  
(2) low volatility which increases safety factors this is desirable for the persistence of the solution on the water surface and decreases evaporation of solvent due to the hot exhaust gases and

(3) non-corrosive and non poisonous chemical properties.  
The methylated naphthalenes were chosen, and in particular a fraction Velsicol NR 70 (Velsicol Corporation Chicago) was readily available a 20 per cent solution of DDT in the latter solvent was used

The optimum size of aerosol droplet deposited on water surface lay between 25 and 50 microns in mass median diameter thus particle size (35 microns) enabled 200-foot swath widths from a height of 30 feet to receive the adequate larvicidal dose of DDT a particle size of under 60 microns ensures adequate penetration of heavy vegetation cover. A deposit of 0.0001 lb. DDT per acre (1 microgramme of DDT per square foot) with a 35-micron particle size killed 90 per cent of 4 *quadrimaculatus* larvae in the open. In practical application the authors recommend the following deposit figures per acre to ensure a 90 per cent 4 *quadrimaculatus* larval kill — Open 0.0005 lb DDT medium cover 0.0025 lb DDT high cover 0.005 lb DDT. A table is given showing the widths of 90 per cent larval kill which will be obtained under varying rates of plant cover aerosol discharge and flight pattern.

[This paper is a valuable contribution on this method of anopheline control.]  
R Ford Treckle

BEKLEMISHEV V N, SILEKOVA, M F & ORLOV P M. [Experiment on the Determination of the Necessary and Sufficient Radius of Antilarval Treatment.] *Med Parasit & Parasitic Dis* Moscow 1945 [1948], v 14 No 6 3-8 fig. [In Russian]

A knowledge of the size of the area to be covered in undertaking anti-larval measures for the protection of a given site against malaria is of great practical importance. If the radius is too small mosquitoes continue to enter the protected zone. If it is excessive considerable unproductive expense is involved. In general, the area of the protected zone is proportional to the square of its radius. The actual practice varies according to local conditions. In the case of *Anopheles maculipennis* a width of 3 km. is considered to be sufficient but in the tropics it is usually reduced to 1.6 km. while in Russia it is sometimes extended to 5 km.

Working in the flood area of the Volga, near Kuibyshev in 1940 and 1941 the authors carried out experimental field observations on this question. The problem was to determine the effect of the width of a controlled zone surrounding a settlement, which it was desired to protect upon the influx of mosquitoes into the settlement in other words to ascertain the rôle of each concentric belt around the settlement upon the mosquito density in it. With this end in view an estimate was made of the density of larvae in an area with a radius of 3 km. from the settlement after which complete anti-larval measures were undertaken in all the breeding places within three concentric zones, each 1 km. wide in succession. Originally the zones with a radius of 1 and 2 km. were found to have a uniform density of larval population while in the outer zone (radius 3 km.) the density was much lower. After the first kilometre zone

had been dealt with the larval density within the second kilometre zone was doubled whereas in the third kilometre zone it increased only after treatment of the second zone. This centrifugal increase was probably due to dispersion of female mosquitoes from the water-collections treated with petroleum. While the increased density of the second zone following treatment of the first zone almost compensated for the depopulation of the latter the density in the third zone was unable to keep pace with the losses caused by anti-larval treatment of the first two zones.

The results of these operations were correlated with an estimate of the density of adult mosquitoes within the settlement based on counts made in three control sites. After treatment of the first zone the mosquito density in the settlement was reduced by 82.4 per cent. After treatment of the second zone it fell to 0.3-0.4 per cent of the original density. Thus thorough larval destruction within a radius of 2 km, almost completely stopped the influx of active females (*A. maculipennis messeae*) into the protected settlement. From this experiment it would seem that the clearance of a zone within 2 km from the protected area was sufficient. However it is pointed out that in this instance the mosquitoes might have been deflected by two other villages within the area of operations and by cattle in the vicinity. It is concluded that whereas in individual cases anti-larval measures might be limited to a radius of 2 km in other cases it is advisable to cover 3 km. C. A. Hoare

KNISELY M. H. STRATMAN THOMAS W. A. ELIOT T. S. & BLOCH E. H.  
Knowlesi Malaria in Monkeys. I. Microscopic Pathological Circulatory  
Physiology of Rhesus Monkeys during Acute *Plasmodium knowlesi* Malaria.  
A Motion Picture. J. National Malaria Soc. Tallahassee Fla. 1943  
Dec. v. 4 No. 4 285-300 [Numerous refs.]

In previous papers this *Bulletin* 1943 v. 40 584] the authors have described the results of investigations carried out by a special technique on the behaviour of blood and the blood vessels in living *Macacus rhesus*. The observations were made on normal monkeys and on monkeys suffering from *P. knowlesi* infection. The results throw light not only on the pathology of malaria but also on the normal physiology of the blood and blood cells. To render these findings available to students and others interested in the subject the authors have prepared a film. It is a 16-millimetre silent Kodachrome picture about 1,500 feet long on four reels and takes from sixty to eighty minutes to project. It was taken through the microscope at magnifications of 32, 48 or 96 diameters. It shows the normal physiology of the blood and the changes which occur when there is a malarial infection leading to the formation of clumps of infected cells which not only impede the circulation but also lead to a condition of anoxia. Finally the effect of atebirin in disintegrating the clumps is shown. The paper describes the film in considerable detail and points out that it is available on loan to medical schools, medical societies, medical officers of the military services and research groups. Applications should be made to Dr M. H. KNISELY, Department of Anatomy, University of Chicago or to Dr T. S. ELIOT, Department of Anatomy, University of Tennessee, Memphis. C. M. Pennyon

EXEMPLARSKAYA E. V. [Therapeutic Effect of the Cytotoxic Anthraticular Serum in Malaria of Monkeys (*Macacus rhesus*)] *Ved. Parazit. & Parazit. Dis.* Moscow 1945 [1946] v. 14 No. 6 34-7 [17 refs.] [In Russian.]

In recent years the Russian physiologist BOGOMOLETZ has developed a method of stimulating the defence phagocytic functions of the reticulo-endothelial system with the help of a so-called 'cytotoxic antireticular serum'.

which is produced by immunizing an animal with emulsion of RE tissue of another see *Bulletin of Hygiene* 1944 v 19 823].

In view of the predominant part played by phagocytosis in the defence mechanism of the host in malaria the author tested the therapeutic effect of cytotoxic serum in monkey malaria. The experiments were carried out in *Macacus rhesus* *Macaca mulatta* infected with *Plasmodium insus* while the cytotoxic serum was produced in rabbits immunized with an emulsion of spleen and brain from monkeys (homologous antigen) and from dogs (heterologous antigen). The titre of the cytotoxic serum of rabbits was determined by the complement fixation test and the serum was considered to be suitable at a titre not lower than 1:100. It was injected into the experimental monkeys intravenously in doses of 0.05, 0.1 and 0.2 cc. before simultaneously with, and after induction of infection. Control monkey either received normal heterologous serum or were infected without any serum. The therapeutic effect of the cytotoxic serum was determined on the basis of the following indications: (1) intensity of parasitaemia and severity of clinical symptoms; (2) temperature reaction; (3) stimulation of activity of reticulo-endothelial cells; (4) haematological picture; and (5) relapses.

The parasite rate was based on a count per 1 000 red cells. The most severe form of malaria, both clinically and parasitologically (8 per cent infected red cells) occurred in monkeys which received the maximum dose of serum (0.2 cc.). It was milder in those which received 0.1 cc. of homologous serum (parasite rate 2.8 per cent) while those injected with the minimum dose (0.05 cc.) had a very mild abortive infection with a parasite rate below 1.5 per cent. The heterologous cytotoxic serum had a relatively slight effect upon the reduction of parasitaemia. Among the control monkeys in those given 0.05 cc. of heterologous serum the course of the disease was as severe as in those without serum while only a light reduction of parasitaemia occurred in those which had 0.1 and 0.2 cc. serum.

The blood picture as well as the clinical symptoms corresponded to the severity of the disease. The effect of the serum treatment upon relapses was similar to that upon the parasite rate i.e. the higher the dose the greater the liability to relapse no relapses having been observed in monkeys treated with the minimum dose of serum (0.05 cc.).

It is concluded that treatment with cytotoxic antireticular serum leads to a stimulation of the defence phagocytic function of the reticulo-endothelial system in infected monkeys which results in a suppression of all manifestations of the infection, the maximum effect being produced by the lowest doses of the serum.

C. A. Howe

HAAS V. H. WILCOX Aimee & EWING Frances M. Infection of Chick Embryos with Non-Pigmented Forms of *Plasmodium gallinaceum*. *J. National Malaria Soc.* Tallahassee Fla. 1945 Dec., v 4 No 4 279-84

The authors show that inoculation of an emulsion of brain substance containing exoerythrocytic stages of *P. gallinaceum* into the yolk sac of developing chick embryos leads to infections which are chiefly of exoerythrocytic forms. Erythrocytic forms are either absent or few in number. It has also been shown that subinoculation with emulsions of the brains of infected embryos leads to the same type of infection. Seven serial passages have been made in this way so that it would seem that a preponderating exoerythrocytic infection could be carried on indefinitely. In a certain number of chicks which hatched and were found to be infected, the infection was of the same type. As regards the erythrocytic forms in the embryos it was noteworthy that many of these were without pigment. It is thought that these pigmentless forms are directly

developed from merozoites of exoerythrocytic forms. As chicks inoculated with blood of embryos containing pigmentless erythrocytic forms develop infections of the ordinary type in which the erythrocytic forms contain pigment it is assumed that in the embryos or in the chicks found infected when hatched the pigmentless forms would have acquired the power of forming pigment had the hosts lived long enough for several cycles to have occurred. C M Wenyon

HUFF C G & COLLSTON F The Relation of Natural and Acquired Immunity of various Avian Hosts to the Cryptozoites and Metacryptozoites of *Plasmodium gallinaceum* and *Plasmodium relictum* *J Infect Dis* 1946 Mar-Apr v 78 No 2 99-117 3 figs [25 refs]

When chickens are infected with *P. gallinaceum* by blood inoculation after an incubation period the length of which depends on the dose of infected cells administered there develops an infection the intensity of which varies with the size of the inoculum. Exoerythrocytic forms begin to appear at about the eighth day and they reach a maximum at about the 25th day. The chickens may die at this stage though very few or no erythrocytic parasites are present in the blood following the falling off of the blood infection at the crisis. A relapse of the blood infection of short duration may occur and if the bird survives the exoerythrocytic stages are rapidly reduced. When sporozoites are injected instead of blood blood infections result whose intensity varies with the dose. When the dose of sporozoites is small the resulting blood infection may be difficult to detect. In any case there is an incubation or prepatent period which varies little (5 to 8 days). Following the injection of sporozoites pre-erythrocytic stages are very abundant in the tissues. When canaries are inoculated with blood or with sporozoites no blood infection occurs and exoerythrocytic stages cannot be found in the tissues. The canary is therefore completely immune to *P. gallinaceum* infection.

Ducks and geese occupy an intermediate position. Blood inoculation produces a transient blood infection but no exoerythrocytic stages can be found. When sporozoites were injected, geese showed a transient parasitaemia but the presence of parasites in the blood of the duck was demonstrable only by inoculation of 1-5 cc of blood into chicks. In ducks following blood or sporozoite inoculations parasites might persist in the blood as proved by chick inoculations for as long as 8 months. No exoerythrocytic stages could be found in the tissues. Some experiments carried out with guinea fowl showed that those birds behaved in the same way as the ducks. These observations showed that ducks, geese and guinea fowl occupied an intermediate position between chickens and canaries as regards susceptibility to *P. gallinaceum*.

It was of interest to discover whether this relative immunity of these birds had any influence on the development of sporozoites. When sporozoites are injected into the skin of the wing of chickens their development into cryptozoites and metacryptozoites (pre-erythrocytic stages) can readily be followed at the site of inoculation. When this is carried out in ducks and geese the complete development takes place as in chickens. In canaries as noted above no such development occurs. It seems clear that the natural immunity of the duck and goose which influences the blood infection has no effect on the development of the pre-erythrocytic stages. Attempts were made to render three ducks more susceptible by inoculating them repeatedly with chicken's blood before injecting sporozoites. In two parasites were seen in the blood in small numbers during three days. In some cases at least these parasites appeared to be in chicken erythrocytes. Conversely attempts to reduce the susceptibility of chickens by inoculations of duck's blood were not very convincing. When inoculated with sporozoites the chickens developed modified blood infections—an observation

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## TRYPANOSOMIASIS

WILDE J K H & FRENCH M H An Experimental Study of Trypanosoma  
rhodesiense Infection in Zebu Cattle. } Comp Path & Therap 1945  
July v 55 No 3 206-28 12 charts [18 refs]

Six zebu oxen were used in the experiment they had been living for several months in an area which was concluded to be free from tsetse flies and tests made before the experiment began indicated that they had no trypanosome infection.

The Kabamba strain of *Trypanosoma rhodesiense* [this Bulletin 1936 v 33 651] in the blood of heavily infected white rats was injected subcutaneously into the six oxen and all showed trypanosomes in their blood after 7 to 13 days. The trypanosomes appeared irregularly they were polymorphic mostly long forms, and in later only on occasional days they were polymorphic mostly long forms, and in posterior blood corpuscles showed no variations in number that could be attributed to the infection and the haemoglobin content never fell below 82 per cent which is not abnormal in zebu cattle during the dry season when this experiment was made. The red cell sedimentation rate showed little change.

**Plasma proteins**—These were estimated periodically throughout the experiment which lasted for about 8 months the proteins were fractionated with sodium sulphate by HOWE'S technique (J Biol Chem 1921 v 49 93 & 109) and nitrogen determinations were made with the micro-Kjeldahl method. The variations in total protein non-protein nitrogen and pseudoglobulin were small and irregular and no appreciable change occurred in the fibrinogen the eglobulin increased rapidly reached maximum levels between the 8th and 15th days after inoculation and then steadily decreased but had not reached normal levels after 23½ weeks. The albumin decreased rapidly and reached the lowest levels after 23½ weeks. The authors conclude from these findings that infection with *T. rhodesiense* either (a) caused an increase in the dimensional proportions of the plasma protein molecules or (b) altered the conditions of the plasma so that larger proportions of its proteins were precipitated at lower electrolyte concentrations. These changes could not be compared with those in *T. brucei* infections of oxen owing to lack of data of the latter.

The blood sugar was determined by the method of HAGEDORN and JENSEN (Ugeskr f Læger Copenhagen 1918 v 80 1117) no hypoglycaemia was observed.

Clinical symptoms were slight soon after infection the temperature showed certain fluctuations and some of the oxen had transient malaise but they did not lose weight and never gave the impression of being "fly-struck".

**Pathology**—Six months after the oxen were inoculated, 20 cc of the blood of each was injected on two successive days into a goat three of the six goats (from oxen Nos 33 34 and 35 respectively) showed infection. Two oxen (35 and 36) were then stunned and slaughtered and examined microscopically sections being prepared from many organs no trypanosomes and no pathological changes attributable to the infection were found. Guinea-pigs were inoculated with cerebrospinal fluid of ox No 36 (the stunning produced cerebral haemorrhage in ox No 35) and did not become infected.

The authors conclude that *T. rhodesiense* is only mildly pathogenic to zebu cattle, but that it is reasonable to assume that during at least the first six months of *T. rhodesiense* infection, cattle can act as true carriers of the disease and so are a source of danger to humans when moving from areas where sleeping sickness is endemic to other tsetse fly-infected areas from which

*T. rhodesiense* is absent [An attempt to infect volunteers from the cattle would have been interesting there is of course now no reasonable doubt that wild and domestic animals are reservoirs of *T. rhodesiense* and their importance as such in various areas needs investigation.]  
J F Corson

BURTT E Observations on an Antbear (*Orycteropus afer*) in relation to Infection with *Trypanosoma rhodesiense* Trans Roy Soc Trop Med & Hyg 1946 June v 39 No. 6 529-32

The author discusses his own observations on experimental infection of an antbear with *Trypanosoma rhodesiense* and compares them with those of VANDERPLANK [see this Bulletin 1941 v 38 632] who suggested that the lower the normal temperature of this host before infection (in his case 97°F) the higher was the subsequent transmissibility of the trypanosomes in tsetse flies (in his case 2 per cent had salivary gland infections) and the shorter was the life of rats infected by flies i.e. the greater was the virulence of the trypanosomes (his rats lived on the average 18 days) Burtt points out that though Vanderplank's suggestion is borne out by the short duration of the infection in rats it is not supported by the low transmissibility in the flies. In the experiments conducted by Burtt the temperature of the antbear was 95°F the percentage of flies having salivary gland infections was 1.5 while the average duration of life of rats infected by the flies was 40.5 days. These results agree with those of Vanderplank as regards the low infection rate in the flies but they do not support his contention that transmissibility and virulence of *T. rhodesiense* may be increased by passage through hosts with a low mean body temperature.

C A Hoare

FULTON J D & STEVENS T S The Glucose Metabolism *in vitro* of *Trypanosoma rhodesiense* Biochem J 1945 v 39 No 4 317-20 [23 refs.]

The authors have studied the glucose metabolism of *Trypanosoma rhodesiense* maintained in a medium containing a small amount of serum. Some tests were conducted in a serum-free medium but the trypanosomes did not survive so well with the result that the yield of metabolic products was low. The products isolated were succinic, pyruvic, lactic, acetic and formic acids, glycerol, ethanol and carbon dioxide. The method of detection of these products is described and the possible paths of their production and the results of earlier work on trypanosome metabolism, are discussed.

C M Wenyon

BURTT E Salivation by *Glossina morsitans* on to Glass Slides a Technique for Isolating Infected Flies. Ann Trop Med & Parasit 1946 July v 40 No 2 141-4 10 figs. on 2 pls.

The author has developed a discovery originally made by BRUCE that tsetse can be made to salivate on a cover slip. If the fly has a salivary infection the trypanosomes are deposited and may be stained and studied. The chance of finding them is increased if the cover slip is smeared with egg albumin.

Burtt finds that the method is a relatively quick and simple way of identifying those individual flies with a salivary infection of *T. rhodesiense*. The method, if repeated on several days, reveals infections which are missed if each fly is fed on a separate rat (which must then be isolated and observed over a period, a laborious method).

Burtt has observed bacteria in saliva, in a very small proportion of flies. The bacteria (which are of several morphological types) may occur in the presence or absence of trypanosomes, though significantly more frequent in their presence. The bacterial infection in the fly is persistent but apparently harmless.

P A Burton

CHABREY M & MABATTE J Les grands suspects de trypanosomiase dans les environs d'Ebolowa (Cameroun) [Suspected Sleeping Sickness Cases in the Region of Ebolowa, French Cameroons.] Bull. Soc. Path. Exot. 1946 v 39 Nos 5/6 189-93

Sleeping sickness does not occur in the Ebolowa subdivision to the same extent as in other parts of the French Cameroons although it has been of serious consequence for the past 20 years in the Nyong Valley only 100 km. away. In 1942 no more than 212 persons were found to be infected among 45 000 examined in the subdivision and three peculiarities were noted at that time — (1) the occurrence of cases clinically resembling sleeping sickness but in which trypanosomes could not be found in the blood, gland juice or c.s.f. (2) extreme paucity of tsetse fly and (3) the high proportion of cases whose infections were acquired in other regions.

It is not uncommon to find patients whose c.s.f. is grossly abnormal and the question repeatedly arises whether such cases in which the patients are suspected of suffering from sleeping sickness, are not in fact cases of syphilis. In order to investigate this problem the authors decided to keep under observation in the Ebolowa Hospital for one year 28 patients suffering from chronic nervous (and in most cases mental) disturbances. Only two of these patients came from outside the region.

Examination of the blood, even after provocative injection of sodium thio-sulphate or other substances consistently failed to reveal trypanosomes, except in one patient who had been ill for three years and whose c.s.f. was grossly pathological. Bone marrow examinations revealed no trypanosomes in any case.

In 18 of the patients the cell-count and albumin-content of the c.s.f. were markedly increased, but this picture improved (though only for a month or two) after trypanamide in the 13 cases so treated. The authors consider this (with doubtful justification) to be strongly suggestive of sleeping sickness as the correct diagnosis.

The Verne reaction which is ordinarily negative in trypanosomiasis uncommonly being syphilitic was positive in only three out of eight cases suspected of being syphilitic.

The most interesting clinical feature of the entire group was the frequency of hemiplegias. This was the presenting condition in 12 of the cases. It was of sudden onset together with fever and headache and tended to improve in most cases without any treatment but leaving the patient after several months with characteristic residual impairments of these and the remaining cases are fully described, and the authors conclude that the variety of signs, and the impossibility of systematizing them, can only lead to the conclusion that they represent more or less intense and irreversible disseminated lesions attributable to a trypanosomal encephalitis possibly due to the well-known diffuse perivascular infiltration of sleeping sickness.

Nearly all the cases which most strongly suggested nervous trypanosomiasis responded rapidly to trypanamide but relapses were frequent and some such patients died, to all appearances as cases of sleeping sickness. In the absence of specific treatment the patients progressively deteriorated. In the absence of anti syphilitic treatment hardly ever gave encouraging results.

The authors feel justified in diagnosing sleeping sickness in most of these cases, on general clinical grounds, as well as by a process of exclusion of other diseases. The epidemiological peculiarity is that in a region free from endemic sleeping sickness there are always to be found a small number of cases

of this disease in which trypanosomes cannot be seen. Where when and how did these persons become infected? The authors discuss various possibilities without reaching any definite conclusions.

The clinical differentiation between trypanosomiasis and syphilis is not always as clear-cut as is often supposed. The fact that classical tabes and G P I are still unknown in the area under review does not mean that central nervous system syphilis does not occur. Syphilitic myelitis cerebral arteritis and meningitis undoubtedly do occur though rarely and four of the present series were found to be syphilitic. The diagnosis of syphilis is however often reached too hastily. If one carries out serological tests among indigenous patients formerly given insufficient treatment on a diagnosis of syphilis one rarely finds unequivocal positive reactions coinciding with nervous troubles characteristic of that disease.

The authors discuss other possible causes of the conditions they have observed. They write that the neurotropism of tropical infectious diseases is as yet insufficiently explored and they admit that their own incursion into the subject is to present rather than to solve a problem which remains for further investigation.

E M Lourie

BELL, F R. & JONES E R. Carbohydrate Metabolism in Bovine Trypanosomiasis. *Ann Trop Med & Parasit* 1946 July, 40 No 2, 199-208 3 figs. [11 refs.]

CARENI A. Divagações otimizadas sobre o porvir de doença de Chagas na América do Sul. [Observations on the Future Significance of Chagas's Disease in South America.] Reprinted from *Arquivos de Biologia* 1943 Sept.-Oct., v 27 No 257 4 pp

ROMERO O dos S. Mais dois casos agudos de doença de Chagas constatados et Pires do Rio Estado de Goiás. [A Report on Two Cases of Chagas's Disease in Pires do Rio.] *Brasil-Médico* 1946 July 20 & 27, 60 Nos. 29/30 243-5 2 figs

MACALHÃES B. F. & FREIRE S. A. Um aspecto electrocardiográfico da doença de Chagas. [The Electrocardiographic Aspect of Chagas's Disease.] *Mém Inst Oswaldo Cruz* 1945 Oct., 43 No 2, 287-89 7 pls. [31 refs] English summary (8 lines)

RANDOLPH N M. DDT for the Control of *Triatoma*. *J Econom Entom* 1946 June, 39 No 3 419

FULTON J D & HARRISON C V. An Outbreak of *Trypanosoma cruzi* Infection in Indian Monkeys. *Trans Roy Soc Trop Med & Hyg* 1946 June, 39 No 6 513-20 6 figs on 1 pl. [11 refs]

The authors report the occurrence in Liverpool of infection with *Trypanosoma cruzi* in six macaque monkeys out of a batch of ten recently imported from India and in two others which had been in the laboratory for two years. The trypanosome had all the morphological developmental and cultural characters of *T. cruzi* which are described in detail. In connexion with experimental work carried out on these monkeys it was possible that in some cases the infection was transmitted from one monkey to another by blood inoculation.

In discussing the possible source of these laboratory infections the authors note —(1) that the ship in which the monkeys had been transported called at a number of ports in South America and passed through the Panama Canal i.e. they had been in the endemic areas of Chagas's disease (2) that a strain of



*T. cruzi* in mice is kept in the same building and (3) that bed-bugs were also discovered there but none was found in the monkey cages and those examined for flagellates were negative. Infection with *T. cruzi* had already been reported from Asiatic monkeys kept in European and North American laboratories on several previous occasions.

To account for such laboratory infections some observers have suggested that the distribution of *T. cruzi* is not restricted to the New World, and that the infections in the monkeys had been naturally acquired by them in Asia. The present authors leave open the question regarding the source of infection in their monkeys but do not exclude the possibility of a laboratory infection acquired in Britain.

[Though the fact is not mentioned in the present paper the reviewer is aware that in at least two of the laboratories to which the authors refer strains of *T. cruzi* are maintained in rodents while in one of them a search carried out after the discovery of *T. cruzi* infection in monkeys revealed the presence of bed-bugs in the animal house. Thus in all these cases of laboratory infection in monkeys the epidemiological factors for the transmission of the infection from the rodents to the monkeys seem to have been present.] The authors conclude that the possibility of *T. cruzi* infection should be borne in mind when working with rhesus monkeys. [This warning might be extended by pointing to the potential danger of the infection being transmitted to human beings by bed bugs under similar conditions.] C. A. Hoare

FRIEDHEIM E. A. H. & BERGMAN Rose L. An Organic Antimony Compound with Curative and Prophylactic Activity in Experimental Trypanosomiasis. *Proc Soc Exper Biol & Med* 1946 June v 62, No 2, 131-2.

Two types of compound both metal-free are known to have a prophylactic effect in trypanosomiasis: (i) the polysulphonated ureide Suramin (Bayer 205 Antypol etc.) and (ii) amidines such as Pentamidine and Stilbamidine. A third type a quinquevalent antimonial is now described. It is a polymerized sodium salt derived from  $\beta$ -(2,4-diamino-1,3,6-triazinyl-6) aminophenylstibonic acid (synonym: melaminophenylstibonic acid).

In mice this water soluble compound is tolerated at a single intraperitoneal dose of 2.5 gm./kgm. and *T. equiperdum* infections are cured by 0.0125 gm./kgm. the therapeutic index therefore being 200.

Two experiments are described to illustrate the prophylactic property of the compound. Five mice were treated intraperitoneally by 0.05 gm./kgm. (i.e. 1/50th of the 100 per cent tolerated dose) and were inoculated 69 days later with *T. equiperdum*. They all remained uninfected. The mechanism of this prophylactic action seems to be based on the fact that the drug is resorbed and eliminated so slowly that a sufficient trypanocidal concentration is maintained in the organism over a considerable length of time. This theory is substantiated by the fact that the  $\beta$ K of the compound is such that the free stibonic acid is precipitated by  $\text{CO}_2$  from solutions of its sodium salt, and after intraperitoneal and intramuscular injections of the salt a white deposit of the free acid can be readily seen for many weeks on the surface of the peritoneum and between the muscle fibres.

The second experiment illustrates prophylaxis against repeated inoculation. A single intraperitoneal injection of 0.3 gm./kgm. was administered to 105 mice. One month later they were inoculated with *T. equiperdum*. None became infected. The test inoculation was then repeated at weekly intervals. All the mice remained free of infection for 50 days from the start of the experiment but infections began to appear thereafter so that by the 100th day about half and by the 164th day all the mice had exhibited the infection. When this did

eventually arise it differed basically from the classical fulminating septicæmic type and was of a chronic nature such as occurs in man and rabbits with parasites appearing and vanishing from the blood at irregular intervals. In this experiment the mechanism of prophylaxis possibly included an immunological factor

E M Lourie

MAYER R. L. & BROUSSEAU Dorothy Development of Immunity to Reinfection during Chemoprophylaxis of Trypanosomiasis with a New Antimony Derivative *Proc Soc Exper Biol & Med* 1946 June v 62 No 2 238-40

The authors have confirmed the claim of FRIEDHEIM and BERMAN [above] that mice treated with a new antimonial,  $\beta$ -(2,4-diamino-1,3,5-triazinyl-6) aminophenylstibonic acid, are protected from infection by *T. equiperdum* repeatedly inoculated over long periods.

Mice treated by a single dose of 0.05 gm./kgm. [route not stated] and subsequently inoculated and reinoculated up to 45 times with *T. equiperdum* remained uninfected for periods up to 330 days but did eventually become susceptible to infection. Such protection lasting two months or more also arose after oral administration of 0.025 or 0.050 gm./kgm. on five successive days.

Two series of experiments as follows were performed in order to show the possible rôle of immunological processes in the protection produced by these means —

1. Normal uninfected mice were treated subcutaneously by 0.05 gm./kgm. Three weeks later serum obtained from these animals was pooled and injected into normal mice which were then inoculated with trypanosomes. Typical fatal infections resulted. The experiment was repeated in exactly the same way except that the initially drug-treated mice had been infected with trypanosomes 48 hours previously. Contrary to the experience with the other experiment the serum obtained three weeks later from these mice was found to protect a further series of mice from infection. Other such experiments showed that the anti-trypanocidal (sic) effect was obtained five days after the treatment of infected mice. These experiments show that the trypanocidal power of the serum of infected mice treated by the antimonial is not necessarily due to the drug persisting in the body but possibly to other probably immunological processes. Similar results are obtained by the use of neoarsphenamine instead of the antimonial.

2. The development of this property of the mouse-blood is probably an effect of successful treatment and subsequent death of the parasites as has been shown by much other previously published work. In support of this the authors found that mice inoculated with trypanosomes (*T. equiperdum*) which had been killed by repeated freezing and thawing were partially protected against infection the protection being manifested by a protracted incubation period on subsequent inoculation of viable trypanosomes.

E M Lourie

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### LEISHMANIASIS

GHOSH H. GHOSH N. N. & RAY J. C. A Preliminary Note on the Complement-Fixation Reaction in Kala-Azar with a Specific Antigen as an Aid to Diagnosis. *Ann Biochem. & Exper Med* Calcutta, 1945 v 5 No 4 153-8 11 refs.]

The authors report very successful results in diagnosis of kala azar by the complement fixation reaction in which an antigen prepared as follows was used.

Cultures of *L. donovani* on Ray's medium [this *Bulletin* 1933 v 30 522] were emulsified with 0.25 per cent. phenol in distilled water. The emulsion, matched with No. 8 of Brown's opacity tubes, showed 80 million flagellates per cc. The emulsion was kept for 25 days in a glass phial in the incubator at 37°C. being taken out each day to undergo mechanical shaking for two hours. At the end of the period the contents of the phial were centrifuged, the supernatant fluid, after filtration, being used as the antigen. The test was carried out with slight modification according to Method 4 of the Medical Research Committee's Report on the Wassermann test (1918). It was found to be highly specific being positive in early cases of kala azar when the usual serum tests are still negative.

C. M. Wennyon

COLLIER H. O. J. & LOURIE E. M. The Action *in vitro* of Diamidines and other Compounds on *Leishmania donovani*. *Ann Trop Med & Parasit* 1946 Apr v 40 No 1 88-100 [25 refs.]

The culture medium employed in the tests described was composed of one part of fresh unheated rabbit serum mixed with two parts of a 12.5 per cent. solution of rabbit red blood corpuscles in isotonic saline. The solution was prepared by taking one volume of defibrinated rabbit blood with six volumes of sterile distilled water adding one volume of 6.3 per cent. sodium chloride solution, centrifuging and discarding the deposit. As the highest temperature at which satisfactory growth of *L. donovani* was obtained was 34°C. it was at this temperature that the tests were carried out. A series of tubes of medium containing two-fold dilutions of a drug to be tested were inoculated with flagellates. The tubes were examined on the fifth day and the lowest concentration of drug giving a negative tube was regarded as the effective dose. A total of 40 compounds, mostly aromatic diamidines or closely related substances, were tested. The only ones showing considerable activity were some, but not all, of the diamidines. Antimonials of known activity *in vivo* such as tartar emetic and neostam, were relatively inactive. As regards the diamidines, there was a fair correlation between activity *in vitro* and the reported activity *in vivo*. Compounds with an *in vitro* titre of one million or more had been found to be effective *in vivo*. The *in vitro* technique would appear to be of some value as a screening procedure, at least in this particular chemical group. The leishmanicidal activity of the diamidines has been studied from the point of view of chemical constitution and compared with the similar study of EWING and his colleagues in 1942 on trypanocidal activity [*Jl Chem Soc.* 1942, 103].

C. M. Wennyon.

KAMEL, A. Leishmaniasis of Eyelid. 14th Rep. Memorial Ophthalmic Laboratory, Giza, Cairo for 1939-1944. 124-8.

Cutaneous leishmaniasis is rarely met in ophthalmology; the author describes three cases. The first had a warty growth along the whole length of the left lower eyelid. The second had a small papule in the centre of the left upper eyelid just above the eyelashes which gradually increased in size and ulcerated. The margins became undermined, but not indurated, and the ulcer was not adherent to the tarsus. The third had an ulcer with a granular surface situated on the left side of the nose and cheek. These cases occurred in localities in which the disease has not previously been seen.

Different forms of treatment are mentioned, of which X-ray treatment and diathermy are said to be the best. [No mention is made of intravenous injections of antimony in the general treatment of the disease.]

E. O. G. Krishna

MÉCHIN R. Quatre nouveaux cas de bouton d'Orient du Tell constantinois traités par la quinacrine locale. [Quinacrine Treatment of Four New Cases of Oriental Sore in the Constantine Region.] *Arch Inst Pasteur d'Algérie* 1946 Mar v 24 No 1 57-9

This is a record of four cases of oriental sore from localities in the neighbourhood of Constantine in Algeria. They are of interest in that they are outside the Sahara area, where the disease is more frequently encountered. The four cases were treated with quinacrine (atehrin) injected into the sores all of which were on the face. For sores not too near the delicate tissues of the eyelids 0.3 gm. of the drug is injected once or twice. For sores on the lids not more than a third of this quantity is injected at one sitting. When the full dose is given healing is rapid cicatrization being complete in three or four weeks. In one case after healing an oedema in the sub-orbital region persisted. This is attributed to the toxic action of the quinacrine on the soft tissues in that neighbourhood.

C. V. Wenyon.

PANJA G. Treatment of Oriental Sore by X Rays. *Indian Med Gaz* 1946 June-July v 81 Nos. 6/7 251

ANVARI M. N. Culture et isolement de *Leishmania tropica*. Leishmanisation prophylactique. [Culture of *L. tropica* for Prophylactic Inoculation.] *Arch Inst. d'Hessarek* Teheran 1946 Jan. v 2 No 2 31-5

Working in Teheran the author describes his technique for obtaining cultures of *Leishmania tropica*. With these cultures he has inoculated 120 persons by scarification or intradermally with a view to protecting them against naturally-acquired disfiguring sores on the face. In 60 per cent. of the cases sores developed at the site of inoculation within 20 days to 7 months. As 85 per cent. of the cases of oriental sore are in children in their tenth year it would appear that protective inoculations should be carried out before this age.

C. V. Wenyon

LEITÃO J. S. Pónos canina. [Canine Leishmaniasis in Portugal.] *Rev Med Vet* Lisbon 1945 v 40 229-43 English summary. [Summary taken from *Vet. Bull* 1946 July v 16 No 7 218. Signed U. F. RICHARDSON.]

Attention is drawn to the prevalence of canine leishmaniasis in Portugal. In Lisbon it has been estimated that 3-4 per cent. of dogs are infected. As a check on the value of diagnostic methods a full investigation was made of a clinical case of leishmaniasis in a dog from Coimbra. Positive results were obtained by examination of smears of tibial bone marrow and of the contents of cutaneous ulcers and the formol-gel and Takata-Ara reactions were positive. Blood liver skin and ungual matrix smears were negative as were serum flocculation and the neostibosan and formol-neostibosan reactions.

PESSÔA, S. B. & BARRETTO M. P. Sobre a localização dos parasitas nos tecidos e a intensidade do parasitismo na leishmaniose tegumentar americana. [Distribution of Parasites and Intensity of Parasitism in S. American Cutaneous Leishmaniasis.] Reprinted from *I Reunião Anual dos Dermatologistas Brasileiros Rio de Janeiro 26-28 Sept. 1944* 1945 123-36 8 figs on 4 pls. [31 refs.]

The authors discuss the distribution of leishmania in the tissues of patients with S. American cutaneous leishmaniasis and the variations in intensity of the infections. They show that the parasite is nearly always intracellular but may

lie extracellularly between cells which have been separated by oedema resulting from subjacent inflammation. The type of cell most commonly infected is the histiocyte but parasites may occur in many other types of cells, including polymuclear leucocytes and fibroblasts. The authors were not able to confirm the statements that parasites may occur in lymphocytes eosinophiles or epithelial cells. As regards the intensity of infections the leishmanias are most numerous in the early lesions which are developing rapidly particularly at the margins of the papule. When ulceration commences parasites may still be numerous before secondary bacterial contamination becomes heavy. In old chronic lesions with intense bacterial invasion it may be difficult or impossible to find them. They also occur in small numbers in the lymphatic glands adjacent to the cutaneous lesions and in the lymphatics leading from them, especially in the nodes which develop along their course. When mucosal lesions appear the parasites are again numerous in the early stages. They become increasingly difficult to find as the lesions become old and when they are secondarily contaminated.

C M Wenyon

PESSÔA, S. B. & BARRETO M. P. Sobre as lesões iniciais na leishmaniose tegumentar americana. [The Initial Lesions in S. American Cutaneous Leishmaniasis.] Reprinted from *J. Revista Anual dos Dermatologistas Brasileiros* Rio de Janeiro 26-28 Sept. 1944. 1945 27-35 9 figs. on 3 pls. [22 reis.]

The initial lesion in S. American cutaneous leishmaniasis is shown to be a papule or nodule which may or may not be pruriginous or painful. Not infrequently there is an accompanying adenitis giving rise to a combined primary infection of the skin and glands. In these primary lesions parasites are usually very numerous. The paper is illustrated by a series of photographs showing the primary lesions.

C M Wenyon

MILLAN GUTIERREZ, J. Leishmaniasis de la piel y de las mucosas. Información General. [Cutaneous and Mucocutaneous Leishmaniasis.] *Medicina*. Mexico 1946 Apr 25 & 26 No. 506 160-69 6 figs.

A general account of cutaneous and mucocutaneous leishmaniasis of Central and South America, intended presumably for the information of local medical men.

C M Wenyon

IRIARTE, D. R. Contribución al estudio de la leishmaniosis en Venezuela. [Leishmaniasis in Venezuela.] *Bolet. Laboratorio Clínico Luis Razetti* 1946 June & 6 Nos. 19/20 355-63 16 figs. [Bibliography.] English summary.

This is an illustrated account of mucocutaneous leishmaniasis in Venezuela with special reference to cases having involvement of the nose, mouth and pharynx. Short histories are given of 13 such cases in patients from 15 to 57 years of age. In the nose the destructive process involves the soft parts and cartilage of the septum leading to depression of the tip of the nose producing a characteristic parrot beak appearance. In the mouth and pharynx the ulceration of the mucosa leads to a thickening of the lips and other affected parts. The chief inconvenience complained of by the patients is nasal obstruction for unlike other conditions involving the nose such as syphilis or tuberculosis there is little or no discharge. As a rule leishmania can be discovered in smears made from the lesions if patient search is made. Thus they were found in all but one of the cases described. When parasites cannot be discovered, the intradermal test of Montenegro is useful in confirming a clinical

diagnosis Treatment has been by intravenous injection of tartar emetic. Certain patients have tolerated daily doses of 0.1 gm. till a total of 2 gm. has been given but actually 0.08 gm. is the highest single dose that can be administered with safety. Under this treatment there has been improvement but not complete cicatrization of the mucosal lesions. In connexion with the transmission of the disease five species of *Phlebotomus* are mentioned as possible vectors. In two (*P. longipalpis* and *P. migonei*) previous investigators have recorded leptomonal infections

C M Wenyon

CERRUTI H A reação intradérmica de Montenegro nas cicatrizes inespecíficas dos leishmanióticos. [The Montenegro Reaction in Non-Specific Scars of Leishmania Patients.] *Arquivos Dermat e Sifilografia de São Paulo* 1945 Sept. v 9 No 3 71-9 [22 refs]

In twenty five cases of cutaneous leishmaniasis in Brazil the author has carried out the Montenegro test on the normal skin the scars of healed leishmania lesions the scars of smallpox vaccination the scars resulting from previous Montenegro tests and scars resulting from other causes. All the tests were positive indicating that the specificity of the test is not influenced by the cicatricial changes in the skin.

C M Wenyon

## FEVERS OF THE TYPHUS GROUP

LOWE J Ten Cases of Typhus in Civilians in Calcutta. *Indian Med Gaz.* 1946 Apr-May v 81 Nos 4/5 171-4

The author briefly describes ten cases of fever of the typhus group seen by him in the last quarter of 1945 at the Calcutta School of Tropical Medicine. Only one case had previously been seen at the school—in 1944—although a sharp look-out had been kept since 1942 because of the known occurrence of cases among British and Indian troops stationed in and near Calcutta.

The diagnosis was based chiefly on the serum-agglutination reactions according to which four were diagnosed as scrub typhus four as murine typhus one as tick typhus and the remaining case the only one that was fatal as of doubtful type. A petechial rash was seen in two cases. No mention is made of any attempt to recover the causative organism.

Eight of the patients had lived in the heart of Calcutta one of these had gone outside the city on fishing excursions another had made a journey to Bombay the rest were not known to have left their homes [but the serological groups to which these or the two patients from rural areas belonged, are not distinguished]. No local eschar was seen. In two cases there was slight general enlargement of the lymph nodes.

No further cases were seen till May 1946 when one patient was admitted for scrub typhus.

John W D Megaw

HABIBI M Etude des lésions anatomo-pathologiques du typhus exanthématique au cours de l'épidémie de 1942-1943 en Iran [Study of the Pathological Anatomy of Exanthematic Typhus in the Epidemic of 1942-1943 in Iran.] *Arch Inst d'Histarek Teheran.* 1946 May No 4 63-75 12 figs. on 2 folding pls [25 refs.]

The opportunity for this study occurred in Iran where in the months January to July 1943 there were 15 500 cases of typhus fever with a fatality rate of 17 to 20 per cent.

The naked-eye and microscopical lesions are clearly described the latter are illustrated by 12 reproductions of photomicrographs. The changes observed were of the usual types.

The author was not satisfied with the results obtained by the Castafeda and other standard methods of staining he recommends prolonged staining (24-48 hours) with Giemsa's stain and differentiation with a mixture of absolute alcohol nine parts and oil of cloves one part.

John W D Megaw

CODELEONCINI E. Le reazioni di Widal e Weil-Felix nella pratica sull'altopiano Etiopico [The Widal and Weil-Felix Reactions in the Abyssinian Highlands.] *Boll Soc Ital di Med e Igiena Trop* (Sess. Eritrea) 1945 v 5 Nos. 5/6 71-84 English summary

The author found that serum retained its agglutinating properties much longer when separated from the clot as early as possible.

He points out that serum when exposed to a hot and dry atmosphere without being sealed up may become so concentrated that the agglutination titre is liable to be considerably increased. He found that when dried clot was the only material available this when reconstituted with serum, yielded titres about one tenth as high as the original serum

John W D Megaw

D IGMazio C & CODELEONCINI E. La reazione di Weigl nel tifo esantematico. [The Weigl Reaction in Typhus Fever] *Boll Soc Ital di Med e Igiena Trop* (Sess. Eritrea) 1945 v 5 Nos. 5/6 199-210 English summary (6 lines)

The authors carried out 7 500 rickettsia-agglutination tests on the lines originally worked out by WEIGL presumably the rickettinal suspensions were prepared from the guts of infected lice

Between 1938 and 1945 a series of 2 650 Weigl tests were performed simultaneously with Weil-Felix tests 1 640 of these were of sera from 368 cases of louse-borne typhus the rest included sera of typhus convalescents healthy persons (vaccinated and unvaccinated) trachoma patients Abyssinian prisoners and persons employed in the laboratory as donors of blood meals for infected or uninfected lice.

The conclusions reached were that although the Weil-Felix test was highly reliable the Weigl test had the advantages of never becoming positive in patients suffering from diseases other than typhus and of yielding a significant response about one day earlier

Apart from the earlier rise and an earlier fall in the Weigl titre the agglutination curves of the two reactions were parallel though the Weigl curve was at a lower level.

John W D Megaw

D IGMazio C. Osservazioni e considerazioni sulla terapia del dermatofasi. [Observations and Discussion on the Treatment of Typhus Fever] *Boll Soc Ital di Med e Igiena Trop* (Sess. Eritrea) 1945 v 5 Nos. 5/6 29-50. English summary (4 lines)

Among the many special forms of treatment tried by the author without obvious success were —convalescent serum autohaemotherapy specific immune serum colloidal carbon intravenously congo red and cyanide of mercury mercurochrome and vaccine therapy A line of treatment which included intravenous injection of vitamin C and intramuscular injection of vitamin B<sub>1</sub> was tried in about 300 cases in Addis Ababa, and the author claims that this caused an obvious improvement in the general condition of the patients and that

the fatality rate was reduced from 24-27 per cent to 12-13 per cent. No absolute claim is made for the efficacy of the treatment but the method was found safe and satisfactory [See also GIUNTA and D'IGNAZIO this *Bulletin* 1939 v 36 989]  
*John W D Megaw*

D'IGNAZIO C & CODELEONCINI E. Le vaccinazioni contro il tifo esantematico in Etiopia con il vaccino di Weigl dal 1938 al 1945 [Vaccination against Typhus Exanthematicus by Weigl's Vaccine in Abyssinia from 1938 to 1945.] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea) 1945 v 5 Nos. 5/6 51-70 English summary (4 lines)

About 40 000 persons were vaccinated in Addis Ababa with a vaccine of which 16 000 doses were obtained from Weigl's laboratory and about 25 000 were prepared at Addis Ababa by workers who were personally instructed by Weigl. The incidence of the disease was greatly reduced among the vaccinated as compared with unvaccinated persons exposed to similar risks though it was suspected that many sub-clinical attacks occurred among the vaccinated. In the cases that were diagnosed the symptoms were exceedingly mild and few complications occurred.

Owing to shortage of the vaccine trials were made of doses reduced to one-half one-quarter one-eighth and even one-sixteenth of the usual amount. Among 10 000 persons vaccinated with these small doses the results did not appear to be materially different from those obtained with full doses

*John W D Megaw*

CODELEONCINI E. Sulla vaccinazione con escrementi di pidocchio infetto di tifo epidemico [Vaccination with the Faeces of Lice Infected with Typhus Exanthematicus.] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea) 1945 v 5 Nos. 5/6 221-8 English summary (2 lines)

The paper contains a description in general terms of the preparation of a vaccine from the faeces of lice infected with louse borne typhus. The vaccine has been found effective in immunizing experimental animals and good results are claimed from the use of the vaccine on 5 000 persons. Anaphylactic disturbances are said to be thrice as frequent as with the standard Weigl vaccine which itself is regarded by most workers as obsolete because of the difficulty and cost of production.

*John W D Megaw*

SMITH P H. The Use of Para-Aminobenzoic Acid in Endemic (Murine) Typhus. *J. Amer. Med. Ass.* 1946 Aug 3 v 131 No 14 1114-17 1 chart. [Refs. in footnotes.]

Para-aminobenzoic acid was given to 29 patients suffering from murine typhus the dosage was 2.0 gm given every two hours with bicarbonate of soda till the temperature fell to normal. A similar number of cases "roughly comparable" served as controls. The average duration of the fever in the treated was 10.2 days and in the controls 13.2 days. There was one death in each group. The treated patient who died was 78 years old the drug was started on the 10th day and was continued for four days till the temperature became normal but the patient died of cardiac failure on the 18th day. Penicillin had been given throughout the illness from the 5th day in doses of 20 000 units every three hours and sulphadiazine was given in doses of 1.0 gm. every four hours from the 5th to the 10th day.

The author suggests that sulphonamides may be harmful he did not regard penicillin as having been helpful.



Caution is advised in cases of kidney or liver damage though no toxic effects were observed from the use of the drug in the present series or in 17 cases of other diseases in which the average total dose was 95 gm. Further trials under more rigorous control are recommended.

*John W D Megaw*

MACKIE T T *et al* Observations on Tsutsugamushi Disease (Scrub Typhus) in Assam and Burma. Preliminary Report. *Trans. Roy Soc Trop Med & Hyg* 1946 Aug v 40 No 1 15-46 3 figs. [39 refs.] Discussion 46-56 2 graphs. [MELLANBY K. SHORTT H. E. SAYERS M. H. P. FAIRLEY N. H. FELIX A. CLARK, R. H. P. HOLLINS C. MACKIE (in reply)]

This paper is essentially similar to the one by the same author and 13 collaborators already reviewed (see this *Bulletin* 1946 v 43 917). The larger and more detailed maps illustrating the present paper are very helpful.

Some interesting points arose in the discussion following the reading of the paper. Dr Kenneth MELLANBY said that after one negative experiment he had been able to confirm the observation that partially fed mites, when removed from their hosts reattached themselves to another host in considerable numbers; he added that badly conducted anti-rat measures might sometimes increase the risk of infection. He mentioned that benzyl benzoate as shown by later work, might be more protective than dibutyl phthalate.

Col. H. E. SHORTT enquired whether the author's findings had thrown any light on the occurrence of different serological types in India, and mentioned that among 65 Weil-Felix positive sera tested by himself in Madras 42 were of the OX19 type 16 of the OXK type and 7 of the OX8 type. The reply was that although a few atypical reactions had been observed there was no evidence of the occurrence of other forms of typhus in the area investigated.

Lt-Col. M. H. P. SAYERS showed two graphs which clearly demonstrated that the disease was definitely seasonal in south-east Asia. The curves of incidence among the troops in 1943, 1944 and 1945 showed a considerable rise in June or July reaching the maximum in August or September gradually falling to a low level by January or February and remaining low throughout February, March, April and May though the season of greatest operational activity was the first half of each year.

Brigadier Hamilton FAIRLEY told how dimethyl phthalate had been found by the Orlando group of entomologists in the U.S.A. to be the best of the known protectives against mites and to be a very effective repellent of mosquitoes; how this had been adopted on a large scale by Australian forces in 1943 and how it came to be replaced by dibutyl phthalate which, however was less repellent to mosquitoes.

Dr A. FELIX stressed the importance of the wild rat as a reservoir of infection and expressed the view that an anti-rat campaign might be even more useful in peace time than anti-mite measures. He quoted R. R. PARKER as an advocate of the opinion that susceptible wild animals were essential to the maintenance of infection in the case of the analogous disease Rocky Mountain spotted fever.

In replying Col. MACKIE did not dispute the evidence of a special seasonal incidence of the disease but emphasized the fact that the disease could occur at any season. He also disavowed any intention of minimizing the importance of rodent reservoirs of infection.

*John W D Megaw*

NOAD K. B. Tsutsugamushi Fever in Natives. *Med J Australia* 1946 July 6 v 2, No. 1 20-21

Details are given of two cases in which tsutsugamushi disease occurred in natives of New Guinea. The *Proteus* OXK titre rose to 1-840 in one case and

to 1-1,280 in the other. Clinically the attacks were entirely in keeping with the diagnosis. Another case was probably of the same kind but it was incompletely observed.

The author [reasonably] suggests that the supposed immunity of natives in affected areas is due to previous attacks. *John W D Megaw*

**Likoff W** Changes in the Cardiovascular System in Scrub Typhus in Early Convalescence *Amer J Med Sci* 1946 June v 211 No 6 694-700  
4 figs

A group of 100 patients whose ages ranged from 19 to 35 years was studied after an average interval of 49 days from the onset of scrub typhus. The febrile period had lasted only nine days on the average. All but one of the patients had been ambulatory for at least 14 days before examination.

Among 30 patients who complained of symptoms of rapid heart beat or other cardiovascular disturbance the pulse rate was over 100 in all but two. Among the other 70 only four had a rate of 100 or more.

An unselected group of 25 patients were tested for exercise-tolerance. 12 of these had a pulse rate which remained 10 beats higher after a resting period of two minutes and only one of the 12 had not complained of cardiovascular symptoms.

Electrocardiographic abnormalities were found in 10 patients all of whom had complained of symptoms. The chief changes found were—bundle-branch block (2) intraventricular block (1) negative T waves in two or more leads (3) splintering of the QRS (3) and secondary-degree heart block (1). In five patients the abnormalities persisted till the end of the period of observation. The most significant changes were in the three patients who had bundle-branch or intraventricular block.

No evidence was found of cardiac failure or organic valvular disease in any patient though systolic bruits were heard in the pulmonic area in six and in the mitral area in two. Electrocardiographic investigation is regarded as the most reliable method of estimating myocardial damage. *John W D Megaw*

**Romko B J** Convalescence from Scrub Typhus. *Bull. U S Army Med Dept.* 1946 Aug v 6 No 2 167-73

A detailed examination was made of 312 patients convalescent from attacks of scrub typhus many of which had been severe. The general conclusion reached is that every patient who survives the attack will make a complete and permanent recovery.

The patients were seen between July 1942 and September 1944 they had already spent an average period of four weeks in hospitals in forward areas of New Guinea. One patient was suffering from a second attack after an interval of 10 months the previous illness had been more severe.

The patients on admission were apprehensive, they expected to be incapacitated for life and anticipated a long period of sick leave. The first step in treatment was to dispel both of these "false beliefs".

The chief findings on admission were—an average loss of weight of 15 pounds a resting pulse rate of 100 or over in 55 per cent. tremors of the outstretched hands in 60 per cent. vertigo in 25 per cent. general or local adenitis in 98 per cent. and pigmentation at the site of the eschar in all the cases, amounting to 70 per cent. in which this lesion had occurred.

After a thorough examination the patients were placed in four different classes according to their fitness for exercise. only 8 per cent. needed temporary bed treatment. During the stay in the convalescent hospital which

averaged 28.4 days all but nine of the patients had been reconditioned and were returned to full duty. Those evacuated for further treatment were suffering from various disabilities unconnected with scrub typhus.

The average period from the onset till discharge to duty was 58.9 days it varied from 30 to 133 days. Except for persistent lymph-node enlargement, all the signs and symptoms had disappeared and no electrocardiographic abnormalities remained.

Prolonged rest in bed is strongly deprecated the author found that convalescence was greatly hastened by starting active reconditioning treatment as early as possible after defervescence.

[Most observers will agree that the attitude of over-caution and pessimism in connexion with scrub typhus has been responsible for wastage of man power and injury to the patients but it must be noted that the fatality rate in the present series of cases had been only 4 per cent. In outbreaks with a fatality rate of 10 per cent or over the results might not have been so remarkably good.]

JOHN IV D MCGRAW

HICKS J D Agglutination Titres with *Bacillus proteus* (OXY) in Human Sera. *Med J Australia* 1946 July 6 v 2 No 1 19-20

Sera from four groups of persons were tested for *Proteus* OXY agglutinins — (a) 96 blood donors in Sydney (b) 100 men from a unit in New Guinea in which no cases of scrub typhus had occurred during the previous five months (c) 104 men from a unit in the same district of New Guinea, in which 29 cases of scrub typhus had occurred during the previous three months and (d) 88 natives from a nearby labour camp.

Between 80 and 85 per cent of the members of all the four groups reacted at titres of 1-20 to 1-40 but in the first two groups only 6 and 3 per cent respectively reacted at 1-60 whereas in the last two groups 15 and 17 per cent reacted at this titre.

The author suggests that these figures may indicate the previous occurrence of infection among the members of the last two groups in the case of group C the infection must have been sub-clinical.

JOHN IV D MCGRAW

BUSTAMANTE M E VARELA G & ORTIZ MARIOTTE C II Estudios de fiebre manchada en Mexico. Fiebre manchada en la Laguna. [Studies in Rocky Mountain Spotted Fever in Mexico. *Rev Inst Salubridad y Enfermedades Trop Mexico* 1946 Mar v 7 No 1 39-48 2 graphs & 1 map [Summary in English by the authors]

The authors report the presence of Rocky Mountain Spotted Fever in La Laguna (Coahuila y Durango) Mexico. The epidemiological and experimental studies based on clinical diagnosis gave as positive results the isolation of two strains of spotted fever virus (western type of the U.S.A.) from two groups of *R. sanguineus* naturally infected.

One strain was obtained from lot 8 formed by 13 adult *R. sanguineus* gathered on the adobe walls and earth floor of a house in Granada. The second strain was obtained from lot 10 formed by three adult females of *R. sanguineus* collected on a dog of the Zaragoza Common. The confirmation of natural infection of these ticks from dogs and now in houses is important for the epidemiology of Spotted Fever in Mexico and adds *R. sanguineus* to the natural vectors of the disease in the Continent.

On the same survey were positive the complement fixation tests with sera from two persons recovered from the infection and with sera from two dogs. Lots Nos. 3 and 13 were collected in mattresses where *Rhipicephalus* lived as *Cimex* do in similar conditions.

The Laguna Region belongs by its geography to the north-central part of the Mexican high plateau which extends to the south-east of United States

MAZZOTTI L. & VARELA, G. Conservación experimental del virus de la fiebre manchada en *Ornithodoros furcosus* [Experimental Maintenance of Rocky Mountain Spotted Fever Virus in *Ornithodoros furcosus*] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1946 Mar v 7 No 1 13-15 [Summary in English by the author]

A strain of virus of spotted fever isolated from Mexico was maintained experimentally during 345 days in *Ornithodoros furcosus*. This tick transmits the infection through the egg at least to the first generation

## YELLOW FEVER.

DE PAULA SOUZA, G. H. Fourth Report of the Expert Commission on Quarantine, Epidemiological Information Bull (UNRRA Health Division) Wash 1946 July 31 v 2 No 14 580-88

The Quarantine Commission of the Expert Committee on Health of UNRRA met in New York on July 10th under the chairmanship of Dr P. G. Stock. The main item of interest in their report is an account of the controlled experiment to test the efficacy of the anti yellow fever vaccine made at the Pasteur Institute at Dakar.

Six hundred French soldiers, none of whom had been outside France or received any inoculation against yellow fever, were divided into three groups of 200 (groups A, B and C). Group A were inoculated by scarification with the Dakar vaccine, group B received the Dakar vaccine plus dry smallpox vaccine by scarification, and group C received Rockefeller 17D yellow fever vaccine by subcutaneous injection. The inoculations were given on July 4th and 5th, 1945, and blood samples were taken on August 9th, 1945, one-third of each sample being sent to Dakar for testing, one-third to the Montana Laboratory of the U.S.P.H.S. and one-third held in reserve. Ninety-two cases showed discrepancies in degree between Montana and Dakar, and the reserve sera were sent for further testing to the Yellow Fever Laboratories in Rio de Janeiro.

Final results showed that 98.94 per cent of group A, 97.93 per cent of group B, and approximately 65 per cent of group C had been immunized. [This last figure is calculated from the detailed analysis of results which is shown in a fuller report on the Dakar vaccine printed in *Epidemiological Information Bulletin* Vol. 2, No. 15, an abstract of which will appear in this *Bulletin* 1947 Jan. Vol. 44 No. 1.] The results from 30 unvaccinated controls were negative in 29 and inconclusive in 1. The Commission therefore recommended approval of the Dakar vaccine under Article VI (10) of the International Sanitary Convention for Air Navigation of 1944.

The Commission also approved the yellow fever vaccine prepared at the South African Institute for Medical Research, Johannesburg (this is of the Rockefeller type). They approved this Institute and the Pasteur Institute at Dakar under Article VI (11) as Institutes for testing the potency of yellow fever vaccine.

The yellow fever endemic areas in Brazil were somewhat modified and an area 10 kilometres round the town of Asmara in Eritrea was excluded from the endemic area, subject to the monthly *Aedes* index remaining satisfactory. The questions of differentiating administratively between endemic and epidemic yellow fever areas, of extending the Convention periods for the incubation of

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smallpox and typhus and of the value of the immunity reaction following vaccination against smallpox were also discussed, but no decisions were reached.

[In *Epidemiological Information Bulletin* Vol. 2 No 16 p 689 a correction is made to a paragraph in the paper reviewed above relating to the delineated area in Brazil. This point is not referred to in the above abstract but the correction reads as follows - Attention is called to a printing error in *Epidemiological Information Bulletin* Vol II No 14 p 584 line 21 instead of 15\ read 3\ parallel of latitude. —Ed

BRITISH GUIANA. Report on the Yellow Fever Control Service of the Medical Department, British Guiana, for the Year 1945, including an Historical Résumé from its Origin to Date. BEVIER, G. M.D. Chief Officer] 26 mimeographed pp with Appendices I & II

It is known that jungle yellow fever occurs in the inland parts of British Guiana in 1930 and 1940. DEATH this Bulletin 1940 v 37 90 1941 v 38 67 reported that nearly 3\ per cent of 506 blood specimens from the interior gave positive protection tests and one-fifth of these positive specimens were from people under 20 years of age. But the positive specimens were entirely from the interior and the point is made that although in the past (up to about 1914) the disease occurred in the coastal areas there is no evidence that it has been endemic there since then. The populated coastal region is separated from the inland jungle area by a wide zone of practically uninhabited country, communication between the interior and the sea is limited to river or air traffic. There is a focus of yellow fever in Venezuela adjacent to the boundary of British Guiana.

The yellow fever control service in British Guiana is concerned most particularly with the control of *Aedes aegypti* on the coast especially in the ports and airports. Georgetown is the last port of call for many ships and aircraft leaving the mainland for the islands and countries to the north. One viscerotony post has been established in the jungle country, and others are projected, but in the meantime mosquito control has been developed.

*Aedes aegypti* is common in Georgetown, and control measures have been in force for some years. A trained staff now exists and public co-operation is fairly good. Inspectors visit all houses and have become proficient in detecting breeding places of *Aedes aegypti* particularly those likely to be overlooked by the householders—viz. water-containers, roof gutters and the like. In the controlled area there are 29 102 premises. This country receives a heavy rainfall of 80-120 inches.

The most useful index of the prevalence of *Aedes aegypti* is given by the premise breeding index which shows the percentage of premises in which breeding is found. This is based on the reports of inspectors, who make weekly visits to the premises in the area. A group of houses which one inspector can visit between Monday morning and Friday evening constitutes a zone. Six zones constitute a District which is under the control of a Chief Inspector who is expected to re-inspect about 10 per cent of the houses in each zone. There are also special services for distributing larvivorous fish, for dealing with high tanks, and with roof gutters, for oiling drains and other collections of water and for classification of mosquitoes caught. Squads whose duty it is to capture adult *Aedes aegypti* have become increasingly important. The most sensitive indication of breeding is the finding of adults in houses, and they can usually be found, if present by trained inspectors. The roof gutter problem has been costly to solve but with special training and equipment periscopes ladders, etc. a great improvement has been made. A serious complication of this problem is

the fact that eggs of *Aedes aegypti* can persist in the dry state for over a year and that they can hatch out within a very short time if they are wetted. In Brazil these dried eggs are killed in gutters by means of a blow flame but in Georgetown the risk of fire was too great for this. The water supply of Georgetown and other places depends very largely on roof collection by gutters and storage in barrels and drums. The latter are also a source of breeding and one of the most difficult tasks has been to enforce mosquito-proofing or sealing of such containers.

Insecticides have been used, especially DDT in houses trains aircraft and motor-cars with useful results. One point brought out is that when DDT is (wrongly) used to spray the air of a room as is the custom with pyrethrum products, the result is not so satisfactory as when it is sprayed on the walls. Records are given of various experiments with DDT. Phenothiazine is useful for water containers—it kills insects in dilutions approaching those of chlorine in drinking water and is harmless [in those dilutions] to higher animals.

Aircraft are inspected and sprayed in quite a large proportion having insects have been found and this is causing concern to public health agricultural and veterinary officials alike though no living *Aedes aegypti* or anophelines were recorded during 1944 and the first half of 1945. Vaccination against yellow fever is available free of charge and any person arriving at the coast from the interior is kept under surveillance for six days.

In 1945 there were 207 persons employed in the Yellow Fever Service including probationer inspectors. The financing of the scheme is explained from September 1899 to October 1 1945 359 688 dollars had been expended mostly from Government and Colonial Development and Welfare Funds but with a contribution from the Rockefeller Foundation. Tribute is paid to the Foundation for the scientific assistance it has given.

Plans for the future are set out and there is an interesting Appendix on yellow fever in British Guiana.

Charles Wilcocks

## DENGUE AND ALLIED FEVERS

HITTI J. K. & KHAIRALLAH A. A. A Report on the Recent Epidemic of Dengue in Beirut, Lebanon, and some of its Complications. *J. Palestine Arab Med Ass.* 1946 July v 1 No 5 150-53

An exceptionally severe epidemic of dengue occurred in Beirut in 1945 when the lateness of the rains and of the advent of the cold weather provided conditions in which the disappearance of the disease was delayed.

Early in the course of the epidemic a tendency to haemorrhage was observed in several patients. Petechiae were often seen. Among the other complications were corneal ulceration meningismus (often) post febrile neuralgia (several cases) otitis media (fairly common) and acute gastritis (many cases). Including deaths from complications the fatality rate was about one per cent.

JOHN W. D. MEGAW

## PLAGUE.

DEVIGNAT R. Aspects de l'épidémiologie de la peste au Lac Albert. [Epidemiology of Plague at Lake Albert.] *Ann. Soc. Belge de Méd. Trop.* 1946 June 30 v 26 Nos. 1/2 13-54 4 figs. [21 refs.]

This publication is an elaboration and application of a theory and scheme already propounded [see this *Bulletin* 1946 v 43 647] which gave a linear

equation  $Q = h [k(i+t) + k(i+t) + 1 \cdot i + t]$  for the determination of the common indices  $Q_1, Q_2, Q_3$  of epidemiologic and epizootic transmissibility of plague. The author himself warns his readers that his is an attempt to systematize epidemiology and that the data obtained will be of the order only of first approximations. Practical applications of the method are given in the second chapter and in the third it is shown how the three fundamental planes of plague activity have been studied. Without attaching exaggerated exactitude to the figures obtained it may be concluded that as regards Lake Albert the conditions there of transmissibility were favourable both on the sylvatic and the domestic plane and that there was no difficulty in passing from the one plane to the other. The persistence or endemicity of plague was thus easy to explain in spite of the long silences that can occur on the human plane. These intervals of freedom from plague are exhibited quantitatively by a fifty fold decrease of the  $Q$  index. Moreover with the arrival of plague on the human plane it is even more difficult for plague to be transmitted by fleas to pass from man to man since the local variety of human flea *Ctenocephalides felis strongylus* is stated not to be a plague vector. Pneumonic plague is expressly excluded from these epidemiological investigations.

GURTA J C PANJA G & CHATTERJEE M. The Effect of Sulphadiazine and Penicillin on Experimental Animal Plague. *Indian Med. Gaz.* 1946 June-July v 81 Nos 6/7 234-5  
Penicillin was found of no value W F Harvey

### BACILLARY DYSENTERY

MACGREGOR, I. Acute Enteritis in Subtropical Climates. *Brit Med J* 1946 Aug 17 225-8 1 graph.

Observation of 435 cases of upper respiratory infection (acute nasal catarrh and acute sinusitis) and 357 cases of acute enteritis (simple diarrhoea not of specific dysenteric origin) over a period of 80 weeks suggested by the close correlation of the weekly incidence of the two conditions that the cause of acute enteritis might be related to the causative organism of upper respiratory infections.

Sandstorms and *khamsins* (the strong wind of Egypt) which produced a marked increase in the incidence of acute exacerbations of chronic rhinitis and sinusitis appeared to cause no increase in the incidence of fresh upper respiratory infections or in that of acute enteritis suggesting thereby that mere mechanical irritation of the bowel does not suffice to explain the enteritis. There also appeared to be no connexion between the incidence of acute enteritis and any one specific ration issue. Sudden cold spells of weather or a sudden fall in the temperature at night however increased not only the incidence of acute respiratory infections but also that of acute enteritis.

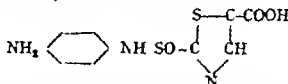
Following the view that acute gastro-enteritis of children is probably due to virus invasion of the intestinal tract rendering the mucous membrane more vulnerable to the ordinary bacterial flora of the region, the author suggests that a similar mechanism might account for the acute enteritis of the subtropics. The absence of an associated gastritis could be explained on the ground that the virus lodging first in the nasopharynx reaches the intestine by invasion of the blood stream that it passes directly from the nasopharynx to the intestine.

through the oesophagus and stomach but that the higher resistance of the adult gastric mucosa prevents the development of gastritis or that in the adult stomach possibly owing to its high pH there are not the organisms to attack the mucosa when it has been damaged.

F Murgatroyd

WINNER P S An Intestinal Antiseptic 2-Sulphanilamido-5-Carboxythiazole  
*Science* 1946 June 21 719-20

2-sulphanilamido-5-carboxythiazole has the formula —



It is a white crystalline solid slightly soluble in water (40 mgm. in 100 cc. at 24°C) giving an acid solution. The solubilities of the mono and disodium salts are greater than 30 per cent. the pH of saturated solutions being 5.4 and 8.5 respectively. The solubility of sodium salt of the acetyl derivative is 8 per cent. so that there is little danger of the kidney being blocked by a deposit of crystals. When tested *in vitro* against bacteria such as streptococcus pneumococcus staphylococcus and enteric organisms its bacteriostatic activity was usually greater than that of sulphanilamide and equal or slightly inferior to that of sulphathiazole and sulphadiazine.

When given in single doses to mice the LD<sub>50</sub> is 8.0 gm. per kgm. by mouth or 5.0–6.0 gm per kgm. by intraperitoneal administration. The chronic toxicity in mice rabbits and dogs was much less than that of the readily absorbed sulphonamides and was comparable to that of succinyl sulphathiazole. When given to man (0.25 gm per kgm per day for 5 days) the blood concentration is always low (less than 1 mgm per 100 cc) about 3–11 per cent of the amount taken by mouth is excreted in the urine. In 4 men taking this dose the number of coliform bacilli in the faeces was reduced to 10–1 000 organisms per gm of wet faeces in 24–48 hours. It is claimed that the new drug is more effective than succinyl sulphathiazole in this respect. HARRIS and FINLAND (*Proc Soc Exper Biol & Med.* 1945 v 53 116) have tried it in cases of bacillary dysentery. they found it to be absorbed into the blood only in small amounts to be non-toxic and to be effective in treating the dysentery.

F Hawking

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

LEITMAN M Z. [The Virulence of various Strains of the Dysentery Amoeba and the Effect of Bile on the Infestation by Protozoa.] *Med Parasit & Parasitic Dis* Moscow 1945 [1946] v 14 No 6 39–44 [In Russian]

With a view to throwing some light on the epidemiological rôle of symptomless carriers of *Entamoeba histolytica* the author carried out a series of experiments to test the virulence of various strains for kittens and pups. The following four strains were used — (1) from a symptomless carrier (2) from a chronic case during the latent period (3 and 4) from cases of acute amoebic dysentery.

The animals (total number 46) were inoculated either *per os*—with cysts or *per rectum*—with the active amoebae. Half of the animals were inoculated without any preliminary treatment whereas the other half received a dose of bile *per rectum* (2 cc. in kittens 3 cc. in pups) preceded by an enema. In the



first group only 11 out of 23 (48 per cent.) acquired an infection, and there was no essential difference in the incubation period, course of infection and intestinal lesions produced by the four strains. However, in the second group (with bile) the results were more striking, the number of infected animals being 16 (70 per cent.) The effect of bile treatment upon infectivity was especially marked in those strains which proved to be less virulent when inoculated without bile in the human carrier. Whereas among 17 rats inoculated without bile only one (5.9 per cent.) became infected in a group of 15 rats treated with bile 5 (33.3 per cent.) acquired an infection.

Bile irritates the mucous membrane of the intestine producing hyperaemia, abundant secretion of mucus and desquamation of the epithelium. These changes apparently sensitize the intestinal wall rendering the experimental animals more susceptible to infection with intestinal protozoa. It is concluded that the results of these experiments have again demonstrated that strains of *E. histolytica* isolated from symptomless carriers are potentially not less virulent than those originating from patients suffering from dysentery. (While this conclusion may be right it should be emphasized that, like previous experiments of this kind, it is based on and applies to the behaviour of *E. histolytica* in non natural hosts)

LINDSEOG G E & WALTERS W. Surgical Aspects of Amoebic Dysentery  
*J Amer Med Ass* 1946 May 11, 131 No 2 92-5 3 figs

This is a report of three cases of amoebic hepatic abscess and one of amoebic granuloma of the caecum occurring among personnel of the U.S. Army and Navy returning after service in the tropics. In one of the cases the abscess perforated through the diaphragm to the pleuro-pulmonary region and in another a right hepatic abscess recurred after open drainage but subsided after a course of penicillin and emetine without further operation. The indications for open drainage in preference to aspiration are discussed. The amoeboma occurred in a patient who had suffered from acute amoebic dysentery twelve months previously for which he had been treated apparently successfully with emetine and carbamone. He relapsed six months later and after further medical treatment with only slight improvement a movable tumour appeared in the right lower quadrant and X-ray studies revealed a constrictive filling defect at the ileo-caecal junction. Right hemicolectomy was performed and was followed by uneventful recovery. In none of these four cases were amoebae or cysts demonstrated in the stools.

W L Harnett

I. SMITH M J. Confusion of Amoebomas with Carcinoma. *Lancet* 1946  
Sept 14 376-8 1 fig

II. HAWK P. Amoeboma and Carcinoma. [Correspondence,] *Ibid* 1946  
Oct. 5 508-9

I. Among the many abdominal cases admitted to the Ministry of Pensions Hospital at Roehampton, London there were some in which left iliac colostomy had been performed for no ascertainable reason. A factor common to all was that they all had suffered from amoebic dysentery and all except one had been treated by emetine injections. The logical conclusion was that an amoeboma had been mistaken for carcinoma. Radical surgery in such cases such as resection of the colon or excision of the rectum may be serious because of the absence of anti-amoebic treatment a fatal outcome is almost invariable.

Occasionally as in the case recorded by MORGAN [see this *Bulletin* 1945 v. 42 124] amoeboma and carcinoma may coexist.

Amoebiasis of skin and subcutaneous tissues may develop after colostomy as in the case cited in this paper. This patient was admitted with the diagnosis of rectal carcinoma. He had served in many countries but had never had dysentery. As the result he claimed, of lifting heavy shells a lump appeared in the left lower abdomen an occurrence associated with diarrhoea, tenesmus and piles. On admission to hospital no amoebae having been demonstrated in the faeces a left iliac colostomy was performed. Subsequently a large infected area appeared in the vicinity of the bowel and further spread was prevented by diathermy excision.

After closure of the colostomy the wound became acutely inflamed and broke down with parting of the sutures in the bowel and re-establishment of the colostomy. During the next four weeks the infected area continued to spread and the patient's condition was rapidly deteriorating when *E. histolytica* was demonstrated in the faeces. On intramuscular emetine treatment reinforced by diodoquin (4 tablets daily for ten days) the stools became clear of amoebae and the wound rapidly scarred over.

Two cases of the converse error are recorded in which carcinoma of the rectum had been treated for dysentery in both rectal digital examination had been omitted.

ii. This correspondent refers to the rare existence of amoeboma of the rectum which may be present as an ulcer or as a papilliferous overgrowth, and which may be indistinguishable from carcinoma.

A course of emetine before resort is had to operation is a valuable aid to diagnosis but only a complete resolution of the amoeboma can be accepted as proof of a purely amoebic origin by this means.

The author has seen six of these cases during four years military service. Five resolved on medical treatment. The sixth was diagnosed as an advanced carcinoma of the rectum colostomy was proposed, but a proctoscopic examination on the operation table revealed the presence of *E. histolytica*. Operation was postponed and the patient died despite a few days of emetine treatment. Post mortem examination showed how futile a colostomy would have proved, for the whole colon was diffusely ulcerated.

Whilst colostomy may be required where other methods fail a note of warning is sounded regarding too hasty embarkation on this procedure owing to the risk of spreading amoebic infection and to serious hepatic complications.

P. Manson Bahr

CROPPER, C. F. J. Amoeboma of the Hepatic Flexure. [Memoranda.] *Brit Med J* 1946 June 29 888.

The case reported is that of a Gurkha, aged 23 with no previous history of ill health. For three weeks he had complained of pain in the right hypochondrium and of evening pyrexia, unaccompanied by bowel symptoms. In the right hypochondrium was a rounded, hard, tender swelling 3½" in diameter which appeared to be unconnected with the liver and was attached to the right rectus. The stools were repeatedly negative for exudate, cysts and ova. The white cell count was 14 000 per cumm. with 80 per cent. polymorphs and sigmoidoscopy showed typical amoebic ulceration, but no scrapings were taken. Skiagrams after a barium enema showed arrest of the barium by a constriction at the hepatic flexure with delayed filling of the ascending colon and caecum and retention of the opaque medium in that part of the intestine after evacuation of the enema. A course of emetine and penicillin led to rapid resolution of the swelling and a skiagram three weeks later showed a normal large intestine.

on sigmoidoscopy all the ulcers were found to be healed. Throughout the illness there were never any dysenteric symptoms.

W. L. Harnett

HALAWANI A. NOR EL DIN G. & AWAT A. Y. Treatment of Amoebic Dysentery with Sulphaguandine as compared with Emetine and other Antidysenteric Drugs. *J. Roy. Egyptian Med. Ass.* 1946 Jan-Feb., v 29 Nos 1/2, 13-18

"(1) Sulphaguandine exerts a favourable effect on the clinical manifestations of amoebic dysentery, but relapses occur shortly after cessation of treatment.

(2) The average time after which relapses occur after sulphaguandine is approximately ten days while this time after emetine treatment is as long as 21 to 27 days.

(3) The action of sulphaguandine is solely on the vegetative forms. The cysts are not affected by this drug. In some cases under sulphaguandine treatment the amoebae changed from the vegetative forms to the cystic stages.

"(4) Resistant cases have been found to benefit from a combined treatment of emetine and sulphaguandine.

(5) The effect of enteronolform and disenteran on the vegetative forms of *E. histolytica* was found inferior to emetine. Their effect was mainly on the cysts."

OSTROVSKY V. G. [On the Protozoal Fauna of the Intestine in Post Dysenteric Colitis (Dysentery Chronica).] *Med. Parazit. & Parazit. Diz.* Moscow 1945 [1946] v 14 No 6 44-6 [In Russian]

The author describes the results of a survey in Stalinabad (Middle Asia) of the protozoal fauna of hospital patients (total 115) suffering from chronic (post-dysenteric) colitis. The examination was carried out mainly in fresh and iodine-treated faecal preparations and sometimes in fixed and stained material. When the results were negative the faeces were examined repeatedly (up to 6 times, and on the average 2.6 times). Only 49.6 per cent. of the patients examined were infected with intestinal protozoa in most cases with one or two species (24.3 and 17.4 per cent. respectively). The relative incidence of the various parasites was as follows: *Entamoeba coli* 20.9 per cent. *Chilomastix* 20 per cent. *Trichomonas* 18.3 per cent. *Giardia* 12.2 per cent. *Iodamoeba* 7.8 per cent. *Endolimax* 4.3 per cent. *Entamoeba histolytica* 2.6 per cent.

In the course of repeated examinations the frequency of the occurrence of different parasites in the same person varied, the findings in 257 examinations of 115 patients being distributed as follows: *Chilomastix* 32 times, *E. coli* 29 times, *Trichomonas* 25 times, *Giardia* 23 times, *Iodamoeba* 9 times, *Endolimax* 5 times, *E. histolytica* 3 times. The author compares his findings with those in 743 healthy adults examined during the same period by another worker whose results were as follows: *E. coli* 37.9 per cent. *Chilomastix* 15.8 per cent. *Trichomonas* 16.1 per cent. *Giardia* 17.4 per cent. *Iodamoeba* 22.1 per cent. *Endolimax* 7.9 per cent. *E. histolytica* 0.4 per cent. *Balanulium* 0.3 per cent. This comparison showed that in cases of colitis the finding of *E. coli*, *Iodamoeba* and *Endolimax* is reduced to half, while *Chilomastix* and *Trichomonas* are almost as common in cases of colitis as in healthy intestines. This confirms the results obtained by other Russian workers who found that there was a marked diminution of the protozoal fauna when the normal functions of the bowel were disturbed.

C. A. Hoare.

LEITMAN M Z & VITLINSKAYA I A [Treatment of Carriers of Pathogenic Protozoa.] *Med Parasit & Parasitic Dis* Moscow 1945 [1946] v 14 No 6 46-50 [In Russian]

In view of the epidemiological rôle of carriers of *Entamoeba histolytica* in the transmission of the infection and of the possible transition from symptomless infection to clinical forms of the disease the authors have carried out an experiment on the treatment of cyst-carriers of *E. histolytica* in Tashkent. A preliminary examination of 1 002 persons revealed the following incidence of pathogenic intestinal protozoa: *E. histolytica* 127 (12.7 per cent), *Giardia* 139 (13.9 per cent), *Isospora* 7 (0.7 per cent), *Balantidium* 1 (0.1 per cent). The infected persons were dealt with as follows: one group of *E. histolytica* carriers was treated with yatren (adults had 4 courses of 0.5 gm administered twice a day for 5 days with intervals of 5 days between the courses; children had 4 courses of 0.25 gm a day for 6 days with intervals of 6 days); a second group of *E. histolytica* carriers was treated with osarsol (for adults 5 courses of 0.25 gm, thrice a day for 5 days with intervals of 5 days; children had 5 courses dosage as for yatren); a third group comprising *Giardia* carriers was treated with acrinine [=mepacrine] (adults received 0.1 gm thrice daily for 5 days followed by a 10-days interval after which the same dose was repeated for 3 days again followed by an interval of 10 days and a repetition of treatment for 3 days; children were given 0.1 gm daily for one month).

Throughout the course of treatment the stools of the carriers were examined once a week and subsequently once a month for five months. During the first period of observation *E. histolytica* cysts were still present in 20.4 per cent of carriers treated with yatren and in 14.4 per cent of those treated with osarsol but the percentage of positive results fell considerably in the course of the first three months. However from the fourth month it began to rise again especially in the yatren group reaching 28.6 per cent after five months; i.e. it was higher than during the period of treatment but in the osarsol group an increase of positive findings was noted only after five months. In the group of *Giardia* carriers treated with acrinine there was also at first a diminution in the number of cyst passers followed by an increase after three months reaching 27.7 per cent at the end of the fourth month and 27.5 per cent after the fifth. On the whole in the majority of carriers the treatment was effective for only 3-4 months after which cysts again appeared in over 33 per cent of the cases. It is concluded that carriers among food handlers can be dealt with effectively only if treated at least twice a year.

C. A. Hoare

ACOSTA MATIENZO Josefina Incidence of Intestinal Protozoa among Patients of the University Hospital at San Juan, Puerto Rico. *Puerto Rico J. Pub Health & Trop Med* 1946 June v 21 No 4 369-71 [Spanish version 372-5.]

HALAWANI A. & EL KORDY M. I. A Case of Human Coccidiosis. *J. Roy Egyptian Med Ass* 1946 Jan.-Feb v 29 Nos. 1/2, 32.

MALDONADO J. F. *Isospora hominis* Fantham, 1917, in Puerto Rico. A Report of the First Case observed. *Puerto Rico J. Pub Health & Trop Med* 1946 June v 21 No 4 397-400 2 figs. [Spanish version 401-4.]

*Isospora hominis* occurs in Puerto Rico as demonstrated by the discovery of a case in which the chances of infection were entirely local. The presence of *S. mansoni* obscured the possible effects of the coccidium on the patient, but there is the possibility that his recent intestinal disorders may be ascribed to

this parasite. The course and general character of the infection were similar to those described by most authors but the action of suadim on the coccidiosis was questionable."

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

RAFTI A. Sur la fièvre récurrente sporadique en Iran. Etude expérimentale de *Spirochaeta persica* (deuxième note) On Sporadic Relapsing Fever in Iran. An Experimental Study of *Spirochaeta persica* (2nd Note) Arch Inst d'Hessarek Teheran 1946 Jan v 2 No. 37-42.

The author in collaboration with DELRY [see this Bulletin 1939 v 36, 757], recorded the existence of human relapsing fever in the north and north-west of Iran. They also showed that the causal agent was *Spirochaeta persica* and that it was transmitted by all stages of *Ornithodoros tholozani*.

Subsequently the disease has been found in other parts of Iran and especially in Teheran and 16 cases have been observed at the Hessarek Institute in the last five years. As a rule the patients recovered spontaneously and treatment with novarsenobenzol was efficacious.

The author has studied the infection in guinea-pigs, rabbits, rats, and mice all of which may be infected, not only by the injection of blood containing spirochaetes, but also by the bites of infected ticks. One in five of ticks collected in infected houses produced infection when fed on normal rats. The infection was transmitted hereditarily to the offspring of infected female ticks. Adults were found to be still infective after 1 175 days, and nymphs infected in this stage were stated to be still infective after 1 403 days. Ticks emerging from eggs laid by infected parents were still infective 2 066 days after the parent was infected.

The spirochaete was found to survive in the brain of white rats up to 593 days. In a footnote the author corrects an error in their earlier paper and states that residual infections in the brain of rabbits, guinea-pigs, dogs and sheep have not yet been demonstrated.

E. Hindle

ANDERSON E. S. Penicillin in the Treatment of Experimental Relapsing Fever in Rats. Trans Roy Soc Trop Med & Hyg 1946, Aug v 40 No 1 83-100.

This is a record of experiments carried out to test the effect of penicillin in white rats inoculated with a Cyprus strain of *Spirochaeta recurrentis* which in nature is transmitted by *Ornithodoros tholozani* and is apparently insensitive to arsenicals.

One group of rats was given massive doses of penicillin either at the time of inoculation of spirochaetes or three hours later or at both these times. This treatment was quite ineffective in preventing infection, but an intermittent prophylactic dose maintained three-hourly for 78 hours seemed to prevent the development of the disease.

Once spirochaetes had appeared in the circulation, intermittent dosage did not control the disease, and the persistence of the infection in the brain of a rat was not influenced by relatively huge doses of penicillin administered early in the disease.

The *in vitro* exposure of spirochaetes to high concentrations of penicillin did not affect their structure, motility or infectivity.

Professor S. ADLER and Dr R. ASHBEI (personal communication to the author) using a similar strain of spirochaete have carried out a comparable

set of experiments also with negative results. It would seem therefore that the Cyprus strain of *S. recurrentis* is not only resistant to arsenicals but also to penicillin  
E. Hindle

RANDOLPH N. M. DDT to control the Relapsing Fever Tick. *J. Econom. Entom.* 1946 June v 39 No 3 396

The results as given in table I show that DDT sprays of 10 per cent and 20 per cent strengths were effective in killing relapsing fever ticks. Applying DDT spray directly to the tick does not appear to increase the effect of the insecticide. DDT of high concentrations is a promising insecticide for controlling these ticks however the cost and feasibility of applying it to natural conditions may be prohibitive. Field experiments are being conducted.

DAS GUPTA, B. M. & SEY, R. L. Canine Leptospirosis in Calcutta. *Indian J. Vet. Sci. & Animal Husbandry* 1945 Mar v 15 Pt 1 52-4 2 figs on 1 pl.

A case of leptospiral jaundice in the dog caused by *Leptospira icterohaemorrhagiae* is described.

## YAWS

HALAWANI, A. & NOR EL DIN, G. A Case of Juxta-Articular Nodes in a Syphilitic Patient. *J. Roy. Egyptian Med. Ass.* 1946 Jan.-Feb v 29 Nos. 1/2, 80-83 1 fig.

SOMPATRAC, L. & SPENCE, H. A Yaws Clinic in New Georgia. *Arch. Dermat. & Syph.* 1946 Aug v 54 No 2, 205-6

GUIMARÃES, F. N. Ensaios terapêuticos com penicilina. V. Bouba (Framboesia pian yaws). I. Dose curativa mínima. II. Redução do número de injeções diárias. III. Redução de tempo de tratamento pelo emprego de doses mais elevadas. [Penicillin Therapy V Yaws.] *Mém. Inst. Oswaldo Cruz.* 1945 Aug v 43 No 1 31-58 15 figs. [Summary in English by the author.]

This report belongs to the series of works carried out at Oswaldo Cruz Institute on the treatment of treponematoses with penicillin.

The present report deals with investigations performed in order to ascertain the following points:—(1) the minimal curative doses for the initial lesions of yaws; (2) the effect of reduction of the number of injections each day to verify the possibility of application of penicillin in the prophylaxis of yaws in rural zones; (3) reduction of the time of treatment by application of high doses.

- (1) With doses of 150 and 100 Oxford units every four hours clinical recovery was obtained after 17 days of treatment. With 50 O. u. during 40 days clinical recovery was not obtained.
- (2) (a) With 3 injections of 400 O. u. each day (at 6, 12 and 18 hours) clinical recovery was obtained after 14 to 16 days.
- (b) with 2 injections of 400 O. u. each day (at 6 and 18 hours) clinical recovery was obtained after 16 to 23 days.
- (c) with 1 injection of 1,600 and 3,200 each day clinical recovery was obtained after 30 and 20 days.

[December 1946]

obtained by biopsy showed the usual leprotic tissue with the organisms. When these tumours are numerous little can be done beyond the giving of chemotherapy but if they are few good results may be obtained by removal of them.

H Harold Scott

GRUENFELDER, R. & LASCH W. Leprosy of the Nose in relation to the Sexual Apparatus. *Acta Med Orientalis* (Palestine & Near East Med J) 1946 May 1 5 No 5 156-61 [43 refs.]

The authors have previously found in cases of infantile cryptorchidism anomalies in the olfactory sphere. In the present paper they discuss a similar relationship in cases of leprosy and they quote from a number of writers in support of this view. They have noted, in male lepers effeminate features usually only met with in eunuchs and in nodular and mixed cases remarkably early reduction of sexual functions is to be observed. Those who are attacked before the age of puberty may show arrest in the development of the testis and of secondary sex characters with according to GRUENFELDER, absolute impotence or loss of sexual powers in 85.4 per cent of nodular cases. The sexual apparatus of women in nodular cases is reported to be affected in the same way as in men, with resulting dysmenorrhoea and sterility and in females attacked young there is absence of menstruation later on. It is in just these nodular cases that the nasal mucous membrane is also affected in leprosy as shown by references to papers of older writers. The analogous behaviour of the sexual system and the nose indicates that something in common connects them, but further investigations are required to enable the precise relationship to be determined.

L Rogers

PORTUGAL H & ROCHA, G L. Juxta-Articular Nodes of Leprous Origin. *Arch Dermal & Syph* 1946 Mar 1 53 No 5 471-6 5 figs. [Refs. in footnotes.]

This condition is most commonly seen in syphilis and yaws it has also occasionally been observed in tuberculosis. The author now records a case of leprosy with a nodule the size of a chestnut near the upper epiphysis of the right ulna, together with other leprosy nodules in various parts of the body. On extension and macroscopical examination as shown by illustrations, it was found to be fibrous in nature with numerous capillaries and small cellular infiltrates. The central zone showed numerous lepra cells of Virchow with many acid fast bacilli typical of a leproma.

L Rogers

HARLEY R D. Ocular Leprosy in Panama. A Study of 180 Cases. *Amer J Ophthalmol* 1946 Mar 29 No 3 295-316 19 figs. [37 refs.]

One hundred and fifty cases of ocular leprosy are reviewed by Harley. Twenty-six per cent were classified as belonging to the anaesthetic form and seventy-four per cent were classified as belonging to the nodular and anaesthetic types. Nearly all the mixed cases showed a positive blood test for syphilis whilst the neural cases were less likely to give a positive test unless there was an acute tuberculous reaction. It is generally agreed that lesions of the eye present a very real and serious complication in leprosy and ocular involvement varies from 20 to 100 per cent. of all patients when the different forms of the disease are taken into account. In Panama 80 per cent of the leprosy patients were found to have ocular involvement, not including the adnexa. If the adnexa were included, it may be assumed that in predominantly nodular leprosy all but those in the first few years of their disease had involvement about the

eyes Some form of ocular leprosy will eventually occur if the patient lives long enough. The 10 per cent of eyes free from the disease were found exclusively in recent cases. Among all the organs involved in leprosy, the ocular lesions appeared to cause more complaints than any others.

Not only is the method of transmission of leprosy in dispute but there is still much speculation as to the medium of transfer. The portal of entry for the ocular invasion is also in question. By some it is believed that the bacilli enter the eye externally from the conjunctiva or episcleral tissues. Most workers believe that the ocular infection is secondary to a haematogenous spread. Fuchs found the primary ocular lesions in the anterior part of the ciliary body and major circle of the iris and is of opinion that the bacilli may appear in healthy tissues but do not necessarily affect them. In the case of five sectioned eyes it was shown that inflammation occurred in the perilimbal episclera and the longitudinal fibres of the ciliary muscle extending back to the ora serrata but no further. In all cases the cyclitis appeared to be an older inflammation than the episcleritis which added to the evidence of an endogenous spread. There appear to be two factors exogenous and endogenous which seemed to be acting simultaneously in the disease. In some eyes one factor often predominates over the other. The disease primarily strikes the anterior segment of the eye and it is in this region that bacilli are most often encountered. It is unusual to see any pronounced ocular complication not accompanied by varying degrees of nasal mucous-membrane ulceration and perforation. The possibility of an ascending infection by way of the naso-lachrymal duct is to be considered, but purulent dacryocystitis is not seen as commonly as might be suspected.

In the series of 150 patients 13 per cent. were found to be totally blind in one or both eyes 41 per cent. had vision of 6/60 or less in one or both eyes 43 per cent. had normal vision in both eyes 10 per cent. had normal vision in one eye. Fifty four per cent. therefore may be regarded as the percentage with severe ocular complications of leprosy. The adnexa of the eye, the region of the eyebrows and eyelids are involved with considerable frequency. Fifty per cent. of the patients had hypertrophy of the skin of the brows or cutaneous nodules with varying degrees of loss of hair of the eyebrows or lashes (madarosis). In nodular leprosy formation of nodules about the outer eyebrows is common. The margin of the eyelid usually the upper may be attacked by nodules and these nodules may ulcerate a diffuse infiltration of the eyelid margins may occur which gives the edges a rolled thickened appearance (tylosis).

In anaesthetic leprosy isolated areas of diminished or absent sensitivity occur in the skin about the eyes. These may differ slightly in colour from the rest of the skin. In 10 per cent of cases there was paresis of the orbicularis palpebrarum (lagophthalmos) to the extent that there was incomplete closure of the lids. Fully another 10 per cent of patients showed weakness of the lid closure. In each case the involvement was bilateral but differed in intensity between the right and left side. The cases of lagophthalmos were in the purely neural and mixed types alike. The affection appeared to be a pure neural one and involved the eyelids out of proportion to the other structures. Ectropion resulting from lagophthalmos was found in most of these cases. Exposure keratitis and excessive lachrymation are also the usual sequelae.

Chronic conjunctivitis occurred in 40 per cent. of the cases and was of the catarrhal type with profuse mucopurulent discharge. This caused less inconvenience than one would expect probably because of the diminished sensitivity of the conjunctiva and cornea. Complete absence of sensation of the conjunctiva was however never demonstrated. Nodules on the conjunctiva were found in only two of the 150 cases, and the conjunctiva is apparently more immune than the other ocular structures.



The cornea is the most vulnerable of the ocular tissues and was involved in 67 cases frequently it was the only site in which any pathological change could be seen. The most commonly observed corneal lesion was superficial keratitis which occurred in over 34 per cent. of all cases. This usually began as a light milky haze punctuated by tiny white spots at the superior limbus. The lower margin was well delineated by a wavy line and was 2 to 3 mm. above the pupillary centre of the cornea, so that vision was not impaired. Pannus is usually present. In 23 cases an interstitial keratitis was present. In three cases the giant leprooma occurred this is the most unusual lesion of the cornea. It is engrafted on the cornea from a superficial keratitis and is teeming with lepra bacilli. Beading of the corneal nerves was found in five cases. Corneal anaesthesia was found to be rare.

Second only to the cornea the iris is the structure most frequently involved in ocular leprosy. Iris or its sequelae were recognized in over 50 per cent. of the cases. It was usually bilateral. Iris atrophy is common in the older cases. In old iritis the tiny lepromata were seen in 26 per cent. of the cases. Typically they were greyish-yellow pedunculated pin-point bodies about the pupillary border of the iris. The ciliary body and the anterior choroid were also probably involved but this was more difficult to demonstrate clinically. Cyclitic membranes were found in advanced cases and leprosy involvement of the ciliary body caused destruction of the zonule and subluxation of the lens. Secondary glaucoma is not common contrary to what one might suspect. Leprosy of the sclera is nearly always secondary to limbal involvement. Lens opacities secondary to plastic iritis occurred in 20 per cent. of cases. Ophthalmoscopic examination of the fundi of 50 patients produced negative results, and proved that ocular leprosy is characteristically a disease of the anterior segment.

Prophylaxis for leprosy eyes through protection with dark glasses is advised. Treatment is largely confined to palliative measures. Thyrocin solution (Squibb) used as drops, may be of aid in helping to clear corneal infiltration. The leprosy patient withstands surgery of the eye well, despite the chronic inflammation. Surgery of the eyelids produces gratifying results.

E. O. G. KIRWAN

NEVES, A. *Sarna crustosa. [Scabies in Leprosy]* *Rev. Brasileira Leprologia* S. Paulo, 1945 Dec. v. 13 No. 4 251-60 11 figs. [15 refs.]

[This and the following three abstracts deal with papers read at the Leprosy Congress held at Minas Geraes in June 1945.] Two cases are recorded of the lepromatous type of leprosy associated with scabies infestation. The hands, forearms, buttocks, thighs and legs and, in one case, the left scapular region, were involved. Locally there was incrustation and much itching and the fingers showed deep fissures (clearly depicted in a photograph). The itch mite and also acid-fast bacteria were seen by microscopical examination. Association of scabies with the nervous type of leprosy has also been reported and the author states that the anaesthetic leprotic condition does not affect the infestation by scabies.

H. Harold Scott.

ALEXIO, JOSEFINO & COELHO, J. T. *Considerações sobre a reação de Montenegro em doentes de lepra. [The Montenegro Reaction in Lepers.]* *Rev. Brasileira Leprologia*, S. Paulo, 1945 Dec. v. 13 No. 4 263-6 1 fig.

As regards the intradermal reaction of Montenegro ARANTES has stated [see this *Bulletin* 1942, v. 39 170] (1) That it is always negative in lepers with no history of leishmania infection. (2) that in lepers who had suffered years

before from leishmaniasis it was strongly positive (3) that leprosy does not affect the reaction in patients cured of leishmaniasis (4) that those with leishmania in an ulcer do not give the reaction

The authors have not been able to confirm the last of these statements and quote the case of a leprosy subject aged 39 years of the  $L_1N_1$  type with generalized lepromata and anaesthesia of the forearms hands and anterior surfaces of the knees legs and feet When the reaction was tried a local erythematous papule formed in 24 hours increasing in size and developing a red halo in 48 hours persisting for several days and leaving a small pigmented nodule. The patient had an ulcer 12 cm in diameter near the right tendo Achillis biopsy showed the tissue changes of a leishmanial infection but leishmania were not seen The authors have studied the reaction in 23 leprosy patients and they think it is of possible value in the diagnosis of mixed infections

H Harold Scott

PEREIRA A. C. *Leprosy of the form clinically inapparent. [Inapparent Leprosy]*  
*Rev Brasileira Leprológica* S Paulo 1945 Dec. v 13 No 4 269-72  
 4 figs on 2 pls. [11 refs.]

The case is recorded of a man 20 years of age giving no family history of leprosy who six months earlier had had on the dorsum of each foot raised, symmetrical erythematous lesions which were painful and slightly oedematous. Examination of his nasal mucus revealed the presence of Hansen's bacteria. Within a month the local lesions receded leaving no trace nevertheless the nasal mucus the inguinal gland juice and the lobules of the ears which to all appearances were normal showed the organisms In spite of there being no clinical evidence of leprosy the man was highly infective and all the more dangerous because of the absence of symptoms he was therefore interned, but escaped soon afterwards.

H Harold Scott

DAYEY T F. *Some Observations on the Role of Allergy in Leprosy* *Leprosy Review* 1946 July v 17 No 2 42-62. [46 refs.]

This is a lengthy discussion which is difficult to summarize of what the author characterizes a hypothetical subject because specific antibodies have not yet been proved in leprosy Allergy is best seen in the tuberculoid form and similarities with dermal conditions due to the tubercle bacillus are emphasized The lepra bacillus has feeble pathogenic powers but it can act as an antigen. The early lepromin and the tuberculoid responses are distinct but related indications of the allergic state In a sensitized tissue an effective concentration of antibody in response to the presence of bacilli is produced at an accelerated rate and some diffusion is probable. The young epithelioid cell is said to be the most effective bacteriological element in the tuberculoid response. The appearance of secondary spreading foci indicates a fall of antibody in the skin caused by a decline in sensitivity The work of DHARMENDRA and LOWE indicate that the release of bacillary protein on breaking down of the lepra bacilli is a necessary preliminary to the allergic response and a time-lag may be due to the interval required for this to take place. The antibody must be synthesized in the reticulo-endothelial system of the skin this is a local reaction because one tuberculoid macule may resolve while another spreads at its edge. The author concludes that while allergy is not equivalent to immunity a successful allergic response imparts a degree of local immunity as well as destroying the bacillus

L Rogers

SCHUJMAN S. Estudo comparativo entre a reação de Mantoux e a de Mitsuda nas diversas formas clínicas da lepra. [Comparison of the Mantoux and Mitsuda Reactions in Leprosy] *Rev Brasileira Leprologia* S. Paulo. 1945 Dec. v 13 No. 4 231-6 English summary

This paper deals with observations upon 210 adult patients suffering from leprosy in the city of Rosario.

The object of the investigation was to compare the results of the Mantoux and Mitsuda reactions in the nodular and the nervous-tuberculous forms of leprosy respectively.

Initial grouping divided the patients into 122 cases of the nodular type (Mitsuda negative) and 88 of the tuberculous type (Mitsuda positive).

After performing Mantoux tests on all the patients, the author arrived at the following conclusions —

(1) The percentage of anergy to tuberculin (Mantoux negative 1/10) is higher in the nodular than in the tuberculous type namely 19 per cent. as compared with 3.5 per cent.

(2) The discrepancy arising from the result Mantoux positive and Mitsuda negative is only observed in nodular cases, while in tuberculous cases, the two tests show agreement to the extent of producing 86 per cent. positive results.

(3) The discrepancy between the Mantoux and Mitsuda reactions in the nodular type of leprosy is explained by the existence of specific anergy to *Mycobacterium leprae* on the part of patients suffering from this type of the disease.

H. J. O'D. Burke-Gaffney

MONTI R. Aspects différents du bacille de Hansen dans le sang de lepromateux coloré par la méthode de Macchiavelli. [Hansen's Bacillus stained with Macchiavelli's Method.] *Bull. Soc. Path. Exot.* 1948, v 39 No. 5/6 167-70

This method consists first of staining for two and a half minutes with a 0.25 per cent. solution of fuchsin then differentiating by passing the slide very rapidly through a 0.5 per cent. solution of citric acid and finally counterstaining for a few seconds with a 1 per cent. solution of methylene blue. Specimens of the leucocyte layer of citrated blood from a vein of a case of lepromatous leprosy with bundles of lepra bacilli in large monocytes when stained in this way showed large numbers of clear unstained bacilli seen against the blue background of the corpuscles. In addition a very few short bacilli, only one or two per leucocyte, were found stained vivid red as described in another paper by the same author [see the following abstract]. This finding raised some interesting questions regarding the significance of the very numerous unstained and the very few stained bacilli in such specimens. The author suggests that the unstained ones represent the usual form of Hansen's bacillus furnished with a waxy coat which prevents the action of this stain but the few red bacilli are young forms without a waxy coat, which take the stain. The former may not be able to infect but the latter may be the only infective forms. Their rarity might account for the slight degree of contagiousness of leprosy.

L. Rogers

MONTI, R. Bacillémie lépreuse. Affinités tinctoriales du bacille de Hansen. [Bacillæmia of Leprosy Staining Characters of Hansen's Bacillus.] *Bull. Acad. Méd.* 1948 v 130 No. 9 10 & 11 163-8.

In leprosy the presence of the bacilli in blood should be determined by puncturing a vein through unaffected skin. He advises withdrawing 2 to 3 cc. in sodium citrate solution, and centrifuging. Smears should be made from

the layer of leucocytes because the bacilli are nearly always found in bundles in large monocyte cells although a few may be free in the blood stream. By this method positive results nearly always are obtained in generalized lepromatous cases especially during febrile reactions but never in the author's experience in tuberculoid and trophoneurotic cases. On staining the blood preparations by Macchiavello's method faggots of bacilli may be seen unstained in contrast to a few of a deep red colour in the cells [see the preceding abstract] the stained ones are very short. On staining with heated Giemsa for half an hour the few short bacilli stain to a mallow or mauve colour. *L Rogers*

DE WILDEMAN E. A propos de médicaments antilépreux d'origine végétale  
VI *Senecio* L. [Vegetable Anti-Leprous Drugs] *Inst Roy Colonial Belge—Bull des Séances* 1948 v 17 No 1 317-53

In this long paper the author enumerates 103 species of the genus *Senecio* and the family of Compositae together with notes of the medicinal uses to which they have been put. Alkaloids have been described in a number of them the names of nine of which are given they appear to differ little among themselves and little or nothing seems to be known of their action in the numerous diseases of man and beast for which they have been recommended from time to time. Among the diseases of man referred to are cardiac respiratory liver urinary affections and diseases of the male and female sexual organs. Among general diseases are hysteria, anthrax syphilis and a number of diseases affecting the skin such as ulcers and boils diabetes and leprosy. The only variety mentioned with regard to the last named is *Senecio Kleinia* of the Indies and Canary Islands. The author points out that little is known regarding the precise chemical constituents of these plants some of which are highly toxic. Research is therefore required regarding their true toxic principles and their distribution in different parts of the plants. Until this has been done recommendations as yet made for their uses in medicine must be regarded as preliminary and provisional. The present paper will be useful to anyone undertaking a serious study of the medicinal properties of this genus. *L Rogers*

CALDEIRA R. da Gloria. Contribuição a terapeutica da reação leprotica.  
[A Contribution to the Treatment of the Leprosy Reaction.] *Rev Brasileira Leprologia* S Paulo 1945 Dec. v 13 No 4 277-9

The author has used pituitrin successfully in the treatment of the leprosy reaction.

SLOAN N R. Tracheotomy in Leprosy *Hawaii Med J* 1946, Jan.-Feb v 5 No. 3 125-8, 4 figs.

ROGERS L. Progress in the Control of Leprosy in the British Empire *Brit Med. J* 1946 June 1 825-8.

This is a very full extract of a paper read before the Royal Society of Arts (*Roy Soc Arts* 1946 v 94 525) which deals with the general progress during the last three decades of prophylaxis against leprosy. Reference is first made to the introduction of the modified treatment by injection of suitable products of the old Indian remedy chaulmoogra oils with improved results in early cases only. Next epidemiological work to enable a plan to be formulated whereby early cases may be detected by repeated examinations of close contacts of known cases of leprosy with their treatment on a large scale at out patient clinics. In addition it is essential to success in reducing the incidence

of leprosy to provide agricultural leproseries for the admission and treatment of the advanced infective lepromatous cases under a voluntary system as far as possible the old rigid compulsory segregation must also be modified to allow of out patient treatment of early cases which are otherwise hidden. Successful trials of these methods with the help of the British Empire Leprosy Relief Association founded in 1924 are recorded. Only the fringe of the problem has yet been tackled in view of the number of cases of leprosy in the British Empire now estimated at two million but the way has been opened up for extending gradually the use of the modern methods described. L. Rogers.

FIELDING J W Further Observations on Rat Leprosy *Med J Australia* 1946 May 18 v 1 No 20 681-6

Further experiments on rat leprosy are recorded in this paper. Light natural infections with rat leprosy have been found in one *Rattus norvegicus* and in one *R. rattus*. Other rats are reported to have become infected from excreta containing acid fast bacilli in the mud floors of their cages after a few weeks of contact. Moreover continued inoculation with organisms in excreta results in the production of intracellularity of organisms and in lesions but there was no evidence of typical maximum intracellularity similar to that observed in leprotic lesions. It was also found that carbolized organisms were still viable and capable of undermining the resistance of an animal. Immunization was not obtained by injections of carbolized organisms. After removal from contact with infected soil, rats may become free from infection after 72 days. It is also stated that the infection of rats by rat leprosy is not enhanced by vitamin B<sub>6</sub> deficiency. [The claims made in this and the previous paper see this *Bulletin* 1945 v 42, 603 are based on the assumption that the acid fast bacilli found in the excreta of infected human beings and rats are the true causative organisms of leprotic infections.] L. Rogers

### HELMINTHIASIS

BADIR G Schistosomiasis of the Conjunctiva. *Brit J Ophthalm* 1946 Apr v 30 No 4 215-21 3 figs. on 2 pls.

Schistosomiasis of the conjunctiva is reviewed by Badir and he describes a case which is unique in that it is the first one reported where the worms were observed *in situ* under the conjunctiva. The patient was a boy aged 12 years on examination a tumour of the palpebral conjunctiva of the left upper eyelid was found near the inner canthus. The tumour had been present for more than a month. The swelling was excised and the specimen on examination showed a large number of terminal-spined bilharzia ova [presumably *S. haematobium*]. Many of the ova were degenerated. A male and an included female bilharzia worm were seen lying in a dilated orbital vein.

E O G KIRWAN

KAMEL A Schistosomiasis (Bilharziasis) of the Conjunctiva. *14th Rep Memorial Ophthalmic Laboratory Giza Cairo for 1939-1944* 118-23

In spite of the fact that Egypt is highly infested with bilharzia and that bilharzial granulomata have been found in nearly every part of the body yet bilharzial lesions of the eye are very rare. The ova reach the conjunctiva probably during the migration of young worms some to reach their goal probably wander the wrong way into the vessels of the head to find themselves

in the vicinity of the mucous membrane of the conjunctiva, where they deposit their ova. The ova deposited in the submucosa are seen to be surrounded by an area of digestive rarefaction produced by digestive enzymes secreted by the lateral glands of the embryo. To this zone of rarefaction leucocytes migrate and the eosinophil cells are the most prominent. This is what is called schistosomiasis pseudo-abscess and differs from the ordinary pyogenic abscess in that it does not suppurate.

The lesions may be seen in the conjunctiva as (1) small yellowish pink nodules on the bulbar conjunctiva, single or multiple surrounded by leashes of small vessels and bearing great resemblance to streptothrix nodules of the conjunctiva. (2) polypoid masses arising from the fornices. (3) chalazion-like granulomata on the tarsal conjunctiva. In all forms however one can easily recognize yellowish dots in the centre, not unlike the post trachomatous degenerations of trachoma and if one ruptures and spreads the contents of such nodules on a slide ova can be found by direct examination under the microscope. The lesions are not painful and the patient's attention is usually attracted by the disfigurement. Unlike tuberculosis the preauricular and submaxillary glands are not enlarged in schistosomiasis of the conjunctiva.

One case was seen in which the lesion was bilateral, and cases have been reported from Upper as well as from Lower Egypt. E O G KIRWAN

ABDALLAH A. Bacteriological Flora in Urinary Schistosomiasis. A Report on 150 Cases. *J Roy Egyptian Med Ass* 1946 Jan.-Feb v 29 Nos. 1/2 33-7

FLOCH H & DE LAJUDIE P. Sur les bilharzioses en Guyane française. [Schistosomiasis in French Guiana.] *Institut Pasteur de la Guyane et du Territoire de l'Inini* Publication No 119 1945 Dec. 5 pp [14 refs.]

The authors make the point that most if not all of the few cases of *S. mansoni* infection which have been reported from French Guiana have been acquired outside that country. This infection is endemic in the Antilles, Venezuela, British and Dutch Guiana and elsewhere. *S. haematobium* infection, on the other hand, is not endemic anywhere in the Americas and only imported cases have been seen. Schistosomiasis is not therefore an important disease in French Guiana and the authors have failed to find the common American mollusc host *Australorbis glabratus*. Charles Wilcocks

WELLER T H & DAMMIA G J. The Incidence and Distribution of *Schistosoma mansoni* and other Helminths in Puerto Rico. *Puerto Rico J Pub Health & Trop Med* 1945 Dec. v 21 No 2 125-47 6 figs. [Refs in footnotes.] [Spanish version 148-65.]

A single stool specimen from each of 19 139 Puerto Rican Selective Service registrants was examined for helminth eggs and larvae by a modification of the Telemann acid-ether centrifugation technique. While the group studied was not representative of the total adult male population these findings comprise the first available data on a relatively uniform group of individuals drawn from all sections of the Island.

Helminth eggs and larvae were found as follows. *Schistosoma mansoni* in 1,909 or 9.97 per cent. Hookworm in 10 822, or 56.5 per cent. *Ascaris lumbricoides* in 1,288 or 6.7 per cent. *Trichuris trichiura* in 14 614 or 76.3 per cent. *Strongyloides stercoralis* in 1,984 or 10.4 per cent. *Hymenolepis nana* in 29 or 0.15 per cent. and *Taenia* sp. in 5 or 0.03 per cent. The helminth index was 1.6.

The data were analyzed to obtain information on the relationship of the occurrence of the five common parasites to the age and geographical and occupational distribution of the selectees.

BARROS, J. de R. Determinações nervosas da parasitose sanguínea de Manson e Pirajá da Silva. Forma epiléptica. [Nervous Symptoms in Infestation by *Schistosoma mansoni*.] *Publicações Médicas* São Paulo 1946 Feb v 17 No 7 (199) 43-45-8.

The author states that *Schistosoma mansoni* may give rise to symptoms of involvement of the nervous system varying from general irritability to attacks of vertigo and actual epileptic seizures. He has notes of "some thirty such cases" and gives details of one. The patient was a man of 29 years, seen by the author in 1937. He had had three attacks of malaria since the age of 12 but was generally healthy and strong. There was no evidence of any venereal disease, nevertheless his attacks of abdominal and sacro-lumbar pain, occasional passage of stools with mucus and streaks of blood, vertigo and nocturnal epileptic seizures with loss of consciousness were ascribed to syphilis and he was given antisyphilitic treatment but without any benefit. Examination of the faeces showed cysts of amoeba coli and ova of ankylostomes and of *Sch. mansoni*. After a course of thymol and of foudan, he had no more vertigo or epileptiform attacks and he has remained well. He was last examined in 1945 8½ years after coming under the author's observation.

H. Harold Scott

HERNÁNDEZ MORALES F. & OLIVER GONZÁLEZ, J. Ova of *Schistosoma mansoni* in Purged and Unpurged Faecal Specimens. *Puerto Rico J Pub Health & Trop Med* 1945 Dec. v 21 No 2 209-10 [Spanish version 211-12.]

The authors examined the purged and unpurged faecal specimens of 120 persons, found to harbour *S. mansoni* ova in their stools after a dose of magnesium sulphate. The first faecal samples when no purge had been given, revealed that ova could only be found in 59.3 per cent. of the patients. It is concluded that the ova of this parasite may be found more readily after the administration of a purgative.

TORRES, C. M. & PINTO, C. Lesões produzidas pelo "*Schistosoma mansoni*" no tatu (*Euphractus sexcinctus*) mecanismo de eliminação dos ovos e sensibilidade da espécie animal nas infestações experimentais. [Lesions produced by *S. mansoni* in the Armadillo. Mechanism of Elimination of Eggs. Susceptibility of the Armadillo to Experimental Infection.] *Mem Inst. Oswaldo Cruz* 1945 Oct., v 43 No 2 301-48, 38 figs. (3 coloured) [23 refs.] [Summary in English by the authors.]

"1 The post-mortem examination of a male armadillo (*Euphractus sexcinctus*) experimentally infected by *Schistosoma mansoni* has shown 88 adult female worms and 23 male worms inside the liver and 4 (2 male and 2 female worms) inside the pancreas.

Ova of *S. mansoni* were found in the faeces since the 53rd day after infection persisting till the death of the animal 41 days later.

Schistosomal pseudotubercles are very numerous in the small and large intestine, in the liver and haemolymph nodes. They could not be detected in the lungs, pancreas, heart-muscle, lymph-nodes, kidneys, bladder and testes.

2. Neither cirrhosis of the liver nor polypoid endarteritis and endophlebitis could be demonstrated.

3 In the small intestine ova and schistosomal pseudotubercles remained strictly localized in the submucosa, and none of them was found above the *muscularis mucosae* (i.e. in the mucous coat itself). The small intestine therefore was not related in this particular animal to the elimination of the *S. mansoni* eggs at least at the time in which the post-mortem examination was performed.

4 In the large intestine on the contrary ova and schistosomal pseudotubercles were very numerous in the mucous coat itself and this portion of the gastro-intestinal tract was actually concerned with a very active and widespread liberation of *S. mansoni* eggs.

5 The chief factors affecting the liberation of *S. mansoni* ova as observed in this armadillo are in our opinion (1)—the structure of the large intestine provided with a less regular *muscularis mucosae* as compared with that of the small intestine and larger blood vessels which enter the mucous coat (2)—the extrusion of eggs in the capillaries according to the manner evidenced by KOPFISCH (1937) and their transient fixation in the mucous coat (3)—the formation of a cellular infiltrate about the extruded ova (4)—the histolysis of this cellular infiltrate as well as of the surrounding tissue (5)—disintegration of the walls of the adjoining Lieberkühn's glands as the histolysis increases and consecutive transfer of the eggs to the Lieberkühn's crypt (6)—their further elimination in conjunction with the intestinal juice secreted by the glands.

6 In the small intestine there is an acute catarrhal enteritis probably incited by bacteria or by toxic substances besides a chronic enteritis associated with schistosomal pseudotubercles and eggs.

7 In the large intestine there is a chronic catarrhal colitis associated with schistosomal pseudotubercles and ova, as well as early stages in the development of mucous polyps.

[For another note on the same subject by the same authors see this *Bulletin* 1946 v 43 658.]

MASON P. K., DANIELS W. B., PADDOCK F. K. & GORDON H. H. Schistosomiasis Japonica. Diagnosis and Treatment in American Soldiers. *New England J. of Med.* 1946 Aug 8 v 235 No 6 179-82. [10 refs.]

Four hundred and eighty-one cases of schistosomiasis japonica acquired on Leyte, an island in the Philippines, were studied at an Army general hospital in the United States.

Recurrent epigastric cramps and tenderness were the most frequent complaints on admission but in almost all cases these had disappeared by the time of discharge.

Repeated stool examinations by more than one method were necessary to demonstrate the eggs of *Schistosoma japonicum*. A persistent eosinophilia was suggestive but not diagnostic of continued activity of the disease.

On the basis of comparable series treatment with tartar emetic was found to be much more effective than that with fuadin. Significant toxic reactions with tartar emetic were rare.

It is urged that stool examinations be done repeatedly and by multiple methods on men who have been exposed to this disease so that treatment may be instituted if ova are found.

NAVAL MEDICAL RESEARCH INSTITUTE AND U.S. NAVAL HOSPITAL, Bethesda Maryland 1946 Apr 29 Report No. 1 Biological Studies of Antimony Compounds containing Radioactive Isotopes. III. The Blood-Thru Exchange and Excretion of Antimony in Humans given a Single Dose of Tartar Emetic [SMITH R. E., STORMONT R. T., BIANCO A. A. & EVANS, R. L.] 10 pp with Appendix and 3 figs.



HALAWANI A. & NOR-EL DIN G. Encephalopathy following Treatment of Schistosomiasis with Tartar Ematic. *J Roy Egyptian Med Ass* 1946 Jan. & Feb. v 29 Nos 1/2, 78-8

TUCKER, H. A. Intestinal Cestode Infections in Natives of Panama. *Puerto Rico J Pub Health & Trop Med* 1946 June v 21 No 4 384-5. [Spanish version 366-8.]

1 In a review of 558,566 admissions to Gorgas Hospital Ancon Canal Zone from May 1904 to November 1944 128 instances of intestinal cestode infections were found. Only 15 of these were unquestionably autochthonous in origin

2. The paucity of suitable intermediate hosts together with inspection and thorough cooking of meats were considered the most important factors in explaining this low incidence

3 All parasites found were generally accepted as being cosmopolitan in distribution only 3 species could be definitely considered of local origin—*Taenia saginata* *Taenia solium* and *Hymenolepis nana*

HERNÁNDEZ MORALES, F. Poisoning by Oleoresin of Aspidium. Report of a Case with Post Mortem Findings. *Puerto Rico J Pub Health & Trop Med*. 1945 Dec v 21 No. 2, 213-18 [Spanish version 219-25]

LATIF N & EL KORDY M I. On the Vitamin Content of Hydatid Fluid. *J Roy Egyptian Med Ass* 1946, Jan.-Feb., v 29 Nos. 1/2, 71-5.

DA SILVA, P B. Estrongiloidase. Sintomatologia e tratamento [Strongyloidosis. Symptoms and Treatment.] *Publicações Médicas* São Paulo 1946 Feb. v 17 No 7 (159) 49 51-2.

In 1937 the author had occasion to pass a duodenal tube on a man 23 years of age with signs of duodenal ulcer and he found in the bile and duodenal material abstracted a large number of ova and larvae of *Strongyloides stercoralis*. He was accustomed to treat gastric and duodenal ulcers by daily lavage with 0.1 per cent gentian violet and gave that treatment to this patient. At the end of a week no more worms were seen and the patient felt well.

Some days later a girl of 11 years was seen suffering from severe anaemia and obstinate diarrhoea the faeces contained larvae of *Strongyloides* in large numbers. She objected to the passage of a duodenal tube so the gentian violet was given twice daily in capsules each containing 0.025 gm. for 10 consecutive days. The diarrhoea ceased and the anaemia had improved and examination of the stools failed to reveal any worms. A brother of the last, aged 8 years similarly affected, was cured in the same length of time.

In his conclusions the author states that infestation by *Strongyloides stercoralis* is fairly common in Rio State in the course of about 2 000 duodenal intubations he has met with an average of 30 per cent. infested that the best results in treatment are attained by the introduction of 20 cc. of a 0.1 per cent. solution of gentian violet by means of a duodenal tube, or by capsules of 0.025 gm. of the drug twice a day. If the patient complains of giddiness or malaise after taking the drug it should be given after the chief meals of the day.

H Harold Scott

LANDENBOROUGH, D. Ascariasis causing Acute Intestinal Obstruction. [Memoranda.] *Brit. Med. J* 1946 Sept. 23, 461.

PEEL, E. & CHARDOME, M. Note préliminaire Sur des filariés de Chimpanzés *Pan paniscus* et *Pan satyrus* au Congo Belge [A Preliminary Note on Filarial Worms in Chimpanzees in the Belgian Congo] *Rec Travaux Sci Méd Congo Belge* 1946 May No 5 244-7 4 figs.

The authors report the finding of the adult female *Agamofilaria streptocerca* in *Pan paniscus* full details will be published later

PACHECO-LUNA, R. Notes on Onchocerciasis in Guatemala. *Brit J Ophthalm* 1946 Apr 30 No 4 234-7 [19 refs]

[The author spells Onchocerciasis Onchocerciasis throughout] Onchocerciasis in Guatemala is described by Pacheco-Luna. It was discovered there in 1915 by ROBLES and is endemic principally in regions devoted to the production of coffee and situated at altitudes of 300 to 1,200 metres on the steep slopes of the Sierra Madre. It is estimated that 20 000 persons are infected. Ocular manifestations are observed in 30 per cent. of these and 2 per cent. are blind. The signs of onchocerciasis are classified under three heads—the tumours the characteristic ocular signs which sometimes end in blindness and some rare cutaneous manifestations. The ocular changes are due to a chronic slow and insidious process of sclerosis which takes years to develop. It is caused by the presence of the microfilariae alive or dead, in the tissues of the eye and by the secretions and excretions of both microfilariae and filariae. These act both locally and at a distance possibly by means of toxic products of protein disintegration. The early symptoms are severe photophobia, blepharospasm and a sensation of a foreign body in the eye. At first only a slight ciliary injection is visible but with the corneal microscope a superficial punctate keratitis can be seen. This affects the ends of the horizontal diameter leaving the centre of the cornea free. Later the infiltrations invade the deeper tissues. In some cases whilst the keratitis is in progress but in others independently a plastic iritis develops which seriously affects vision. At first the pupil is contracted. Synechiae and pseudo-membranes develop which obstruct the pupil and force it downwards giving it a pear-shape. The process extends to the nveal tract and degenerated pigmentary lesions of the choroid and retina have been observed. Examination of them is difficult owing to the clouding of the vitreous. In advanced cases the ocular tension is low and the process ends by *phthisis bulbi*. Unfortunately up to the present no therapeutic agent has been found which acts with good results upon the parasites.

E O G KIRWAN

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## DEFICIENCY DISEASES.

CRICKSHANK, E. K. Painful Feet in Prisoners-of-War in the Far East. Review of 500 Cases. *Lancet* 1946 Sept 14 369-72, 2 figs

The author saw 500 cases of this syndrome among British and Australian prisoners in Changi Camp Singapore. It appeared after six months of captivity during which the prisoners had received a diet supplying adequate calories but deficient in first-class protein and in the B group of vitamins. Fresh cases ceased to appear in any numbers and the sufferers gradually recovered, after a few months when there was an all-round improvement in the diet although the quantity of riboflavin supplied remained low. The greatest incidence of painful feet occurred at a time when fresh cases of recognized thiamin deficiency were relatively few.

two important deviations from this were encountered *viz.*—(1) Many stools with a high fat content were well pigmented and not unduly bulky—an observation previously noted [Black and Fourman, this *Bulletin* 1948 v 43 474] further on exposure to light and air pale stools darken in colour and (2) many patients with sprue suffer from attacks of watery diarrhoea (clinical dysentery). The lack of pigmentation in the sprue stool is usually held to be due to the reduction of stercobilin to stercobilinogen but simple dilution of the pigment by fat may be contributory to it. The dysenteric diarrhoea may be due to an intercurrent bacillary dysenteric infection in which case it responds to sulphaguanidine treatment but possibly more often, sulphonamide-susceptible organisms normally commensal become pathogenic in an abnormal gut. Such diarrhoea was observed to yield promptly to parenterally-administered liver extract.

The ratio of split to unsplit fat in sprue usually exceeds the normal 3:1 or 4:1 and this has been attributed to defective absorption of split as opposed to unsplit fat. Bloor (*Biochemistry of the Fatty Acids* New York, 1943) found that normal stools can partially break down neutral fat added to them: the authors find that this lipolytic property is possessed in even greater degree by sprue stools, probably because of the emulsifying action of their high soap content. The lipolytic action was not arrested by penicillin or sulphathiazole, so is not bacterial in origin: it was lessened by the addition of 5 per cent copper sulphate. The relative absorptions of split and of unsplit fats in sprue, therefore cannot be deduced from an analysis of the stools.

The ratios of total split fat and of split fat in the form of soaps in 46 dried stools from ten patients are set out in tabular form. In all but six of these the ratio of split fat present as soaps was found to be over 60 per cent. Irrespective of the total split fat content. Those stools with the greatest content of split fat and containing the greatest amount of soluble soap were the most alkaline—which suggests that the irritant nature of very fatty stools is due to a high content of soluble soaps and not to acidity.

The non-fat dry residue (N.F.D.R.) is composed largely of bacteria and of unabsorbed food residue. On a controlled diet this residue should remain constant but the authors found that after treatment of many but not all of their sprue cases with liver and yeast-extract the N.F.D.R. diminished. The cause of this was not determined but such a diminution in this residue may mask a decrease in the gross fat excretion, the percentage figure for fat in the dried stool as a result of it being unaltered.

With gross variations in steatorrhoea, such as occur in sprue under treatment a fair measure of the water content of the stool cannot be determined by the ratio of dry to wet stool weight: the fatty part of the stool not being wetted. A percentage water content has been calculated from wet weight of stool minus fat and dry weight of stool minus fat, and average figures for 68 stools from 11 patients are given: stools of higher fat content were found to have a higher percentage of water.

In mild or atypical sprue the percentage of fat in the dried stool may be normal, especially if the patient is restricting his fat intake. To demonstrate steatorrhoea such patients must be put on a diet containing 90–100 gm. of fat daily and the stools collected for at least 24 hours and preferably for four days. The fat excreted on such a diet should not exceed 10 gm. daily in a normal person. Where facilities for collecting and weighing stools are lacking, a percentage of estimation of fat in a mixed 24-hour specimen is of more value than an observation on one stool, and a high residue diet must be avoided so as not to mask minor degrees of steatorrhoea. For accurate observations on fat excretion, twelve-day periods of observation are a minimum requisite.

A. R. D. Adams

FRANDSEN S & KRINGELBACH J *Investigations in the Behaviour of the Serum Iron in Hyperchromic Sprue Anæmia. Acta Med Scandinavica* 1946 v 125 No 1 29-39 2 figs [10 refs]

By the term sprue in this article the form more generally known as idiopathic steatorrhoea is probably indicated

Two cases of untreated hyperchromic anaemia in sprue which were investigated immediately after injections of liver showed a reduction of the serum iron value from high normal values to low subnormal values as well as a tendency to persistent low values during continued treatment. The curve thus obtained corresponds to that usually observed in the serum iron of pernicious anaemia during the course of similar treatment. In the first during a reticulocyte rise the peak was reached just after a decrease of the serum iron content had been noted. In the second case decrease in serum iron was more protracted.

In these instances where similarity of the behaviour of serum-iron during the liver treatment of hyperchromic sprue anaemia and that of pernicious anaemia is observed a certain parallelism is to be expected. It appears that no prediction as to the eventual response of the anaemia to specific treatment can be made from the behaviour of the serum iron. In these two cases as a result of treatment the serum-iron fell from normal (high) values—152-170 $\gamma$  per cent and 173-152 $\gamma$  per cent to subnormal values—68 $\gamma$  per cent and 37 $\gamma$  per cent.—respectively analogous to the conditions observed in pernicious anaemia.

P Manson-Bahr

WINGFIELD A L. *Some Observations on the Aetiology and Treatment of Sprue Proc Roy Soc Med* 1946 July v 39 No 9 519-22 (Sect of Med. 15-18) 2 figs. [14 refs]

The author believes that the very rapid response to treatment points to a disorder of function rather than of structure as the basis of sprue. Since 1939 he has made it his practice to permit all patients with sprue to partake of full ward diet and to get up when they wish. They are treated with crude liver injections (Plexan) 4 cc. daily for one week, then on alternate days for one week and twice weekly thereafter and to this is added nicotinic acid 50 mgm three times daily.

A single dose of nicotinic acid 150 mgs is given to test vasomotor and digestive reactions. So far no patient tested has complained of flushing before the beginning of treatments while all patients have given a specific vasomotor response after treatment for two to three weeks. This observation supports the contention that crude liver quickly restores intestinal function. Nine patients were treated on these lines with satisfactory response the average gain in weight has been 27 pounds varying from 13-52 pounds. Stools return to normal in about seven days. Untoward phenomena have been pain at site of injection and transient oedema of the legs and feet has occurred in the second week possibly because of sodium retention.

One extreme case is cited the patient on this mode of treatment doubled her weight.

His experiences have led the author to believe that diet is of little or no consequence in the treatment of sprue. Crude liver extract is important possibly because it is a potent source of vitamin B<sub>12</sub> complex, but it also contains an unidentified fraction which may prove to be the specific factor

P Manson-Bahr

penicillin in a strength of 6 units per cubic centimeter. Treatment was instituted with an ointment containing 5 000 units of penicillin per gram and complete involution occurred after two weeks of therapy. Treatment was then continued for another two weeks to insure permanency of results.

The last patient in this group had been hospitalized almost continuously for the preceding eight months because of a treatment resistant syccous vulgaris. Three million units of penicillin had been administered intramuscularly in eight separate courses and penicillin ointment had been used for three weeks without affecting any improvement. On culture a coagulase-positive hemolytic *Staph aureus* was found, with sensitivity to penicillin in a strength of 20 units per cubic centimeter. Penicillin ointment in a strength of 100 000 units per gram was used and cure was accomplished with three days of therapy. In all treatment was continued for five days and there was not the slightest evidence of local irritation. The patient was followed for another month, but relapse did not occur.

Despite these successes, failures were recorded in other cases, although in some instances penicillin ointment containing 3 330 units per gramme was used, and in one case the ointment was loaded with 10 000 units per gramme. Therefore the authors conclude that even massive penicillin therapy may be inadequate, and may lead to the development of increased penicillin resistance.

Cornia and Alsever consider that the only obvious indication for the administration of penicillin intramuscularly is in cases of severe, widespread infectious eczematoid dermatitis.

In the treatment of 10 patients suffering from pyoderma, sulphadiazine (5 per cent.) was added to penicillin ointment of standard strength (300 units per gramme) the results were disappointing. However benefit did seem to accrue in four patients who received two courses of penicillin locally with an intervening oral course of sulphadiazine.

As the study progressed the filter paper method of bacteriological assessment was given up and the authors adopted, as more accurate a method of assessment devised by COOKE [Bulletin of Hygiene 1945 v 20 497] in which penicillin solutions of varying strength and measured amount (0.1 cc.) are applied evenly to the agar and dried quickly in the refrigerator the organisms to be tested are then streaked across the area and the inhibition of growth, or its absence noted as usual.

As a result of their studies they suggest the following scheme of correlation between the strength of penicillin ointment and the sensitivity of the organisms concerned —

*Strength of penicillin ointment to be used in treatment according to sensitivity of organisms to penicillin*

Sensitivity of Organism		Strength of penicillin units per gramme of ointment
Filter paper method units per cc	Cooke method, units per 0.1 cc.	
1	0.03 to 0.08	500
2	0.1	1 000
4	0.15	3 000
6	0.2	5 000
8	0.25	7 500
10 to 20	0.3 to 0.6	10 000 to 25 000 (?)
20 to 30	0.6 to 1	25 000 to 50 000 (?)
30 to 50	1 to 2	100 000 (?)

R. M. B. MacLEOD.

JACKSON W P U Plant Dermatitis in the Bahamas. [Memoranda.] *Brit Med J* 1946 Aug 31 298

The shrub *Metopium toxiferum* (family Spondiaceae) known as poison wood or poison bark contains a toxin at least as powerful as that of *Rhus toxicodendron*. It flourishes throughout the open spaces of the Bahamas and Southern Florida. The toxin is present in the milk beneath the bark in the leaves and in the fruit and tends to ooze to the surface of bark and leaves producing black stains.

After contact of the skin with this toxic resin there are usually no symptoms for a few days but thereafter small papules are formed which rapidly become vesicular there is itching and surrounding erythema and the lesions usually ulcerate. The rash may spread to distant parts of the body probably as a result of a general allergic reaction of systemic dissemination since blister fluid is not toxic and finger-spread is therefore not likely. The whole process may continue for several weeks. Sometimes the rash is more urticarial with gross erythema and oedema. One drop of the fluid may produce a widespread rash.

Charles Wilcocks

SANTON W J HATCHER F & DERRICK, E. H. Chromoblastomycosis, with Reports of Two Cases occurring in Queensland. *Med J Australia* 1946 May 18 v 1 No 20 695-7 6 figs on 1 pl

Chromomycosis or mossy foot although found in many parts of the world is not common in any country. The authors describe two cases the first to be reported in Australia. In both cases the lesion was a small painless non-inflammatory plaque about 15 mm in diameter with a flattened surface elevated a few millimetres above the level of the surrounding healthy skin. On one patient the lesion which had evolved from a small wart like papule was of 7 years duration and on the other a matter of only 5 months. Topical treatment proved ineffective and excision was practised in both cases. Histologically the lesion was a cutaneous granuloma composed of histiocytes and plasma cells with polymorphonuclear and mononuclear leucocytes numerous giant cells of the foreign-body type and many very conspicuous eosinophil cells. The fibroblastic reaction was very slight but there were marked epidermal proliferations which in neglected cases give rise to the papillomatous character of the lesions. The fungal parasite was seen singly or in little groups scattered throughout the tissue often within giant cells or forming the central object of a little abscess of polymorphonuclear cells. The fungal cells were round or oval from 5  $\mu$  to 14  $\mu$  in diameter averaging 8 to 10  $\mu$  they were of a brown colour thick walled and in some cases septate. Unfortunately the tissues were fixed in formol before the diagnosis was made so the identification of the fungus by culture was not possible.

J T Duncan

PARÁ, M. Histoplasmosis in Brazil. *Amer J Trop Med* 1946 May v 26 No 3 273-82 17 figs [36 refs.]

The author who is a member of the National Yellow Fever Service of Brazil diagnosed five cases of histoplasmosis in the routine histological examination of 169,808 viscerotomy specimens collected in connexion with the yellow fever survey during the period 1939 to 1945. As the diagnoses were made some time after death confirmation by cultivation of the fungus was not possible and the case histories obtained were incomplete. All five patients were children, 2 boys and 3 girls between the ages of 19 months and 9 years. The cases occurred in the following districts: Recreio Minas Gerais, Virrica São Paulo, João Alfredo Pernambuco and Itapé Bahia (2 cases). Four were diagnosed.

In the causation of blindness in all age groups, conjunctivitis and its complications were responsible for 103 out of 254 cases, smallpox for 103, cataract for 28 and glaucoma for 10 cases. Many cases of severe conjunctivitis showed evidence of keratomalacia, a condition which is also very prevalent. [No mention is made of trachoma as a cause of blindness.]

It is believed that at least 80 per cent. of the cases of blindness could be prevented by widespread compulsory vaccination by the provision of a more suitable dietary containing vitamin A and by extending medical facilities in order to ensure that all cases of conjunctivitis should receive adequate treatment.

*Trachoma*.—During the past eighteen years WILSON<sup>3</sup> has had a unique opportunity of studying trachoma from many varied angles and in this article he reviews certain personal observations made during that period. In discussing the aetiology of the disease he states no one has yet succeeded in isolating the infective agent of trachoma in pure culture but there is no doubt that it is a specific infection. He rejects the theories of a lymphatic dyscrasia, adenoidism, nutritional deficiency or similar concepts and does not consider these factors to be predisposing causes.

He regards the evidence in favour of a rickettsia as a cause of trachoma to be far from convincing. *Bacterium granulosis* he regards as the cause not of trachoma, but of a simple form of chronic granular conjunctivitis. He is convinced that typical intracellular inclusion bodies are invariably present in the incipient stages of trachoma and also that, if they are not demonstrable in the early stages of any disease under examination, the disease present is not trachoma. In this connexion it is to be observed that inclusions may be found in the trachomatous conjunctival epithelium some appreciable time before characteristic clinical signs appear in the tarsal conjunctiva but as the disease progresses they rapidly decrease in number and the chances of finding them are correspondingly diminished after the first three months from onset. Therefore while the demonstration of the inclusions in the earliest stages of any doubtful case is of the utmost significance their absence in the later stages is, from the diagnostic point of view, of little importance. There is no doubt now that trachoma is caused by a filterable virus and that the specific infectious agent is demonstrable as an intracellular inclusion body identical with the chlamydozoa originally described by PROWAZEK and HALBERSTADTER.

Wilson discusses the problem of animal experimentation and is of opinion that the ideal experimental animal for trachoma has yet to be found. It would appear that the Sudanese monkey (guet or *Lasiopyga griseocollaris*) is the most susceptible of all the monkeys and apes. When such animals are directly inoculated with trachoma material, mild conjunctival congestion and follicles begin to appear in the upper fornices after a fortnight or so, and sometimes quite a considerable crop of follicles may appear but these gradually retrogress and may perhaps entirely disappear after several months. Appearance of 11 follicles on the tarsus has never been observed, nor does scarring of the conjunctiva or vascularization of the cornea ever take place. Furthermore intracellular inclusions are not found. The position is even more complicated since monkeys may also suffer from a form of spontaneous folliculosis of varying severity which is indistinguishable clinically from the disease produced by the inoculation of trachomatous material and in this disease also intracellular inclusions are not found. BLAND<sup>4</sup> has shown that trachoma can definitely be

<sup>3</sup>WILSON, R. P. Trachoma. A Selection of Personal Observations and Experiences. 11th Rep. Memorial Ophthalmic Laboratory Giza, Cairo for 1939-1941. 15-57. [16 refs.]

<sup>4</sup>BLAND, J. O. W. The Aetiology of Trachoma. A Critical Review of Present Knowledge. 14th Rep. Memorial Ophthalmic Laboratory Giza, Cairo for 1939-1944. 20-106. [58 refs.]

passed from monkey to monkey through man producing all the pathognomonic lesions of the disease and back again to the monkey spontaneous folliculosis is not transmissible in this way. When simian trachoma is transferred to the human conjunctiva typical lesions of the human disease are developed and Prowazek Halberstaedter inclusion bodies are present in abundance. Thus the virus of trachoma although not demonstrable in the conjunctival epithelium of the monkey nevertheless rapidly develops and produces typical colonies after transfer to the human conjunctiva.

In Egypt trachoma is not in the true sense of the word epidemic it is pandemic. It makes its appearance at all times of the year and may be found in 100 per cent of the village population and only to a slightly less degree in the big towns. The disease develops in children before they are a year old and is invariably preceded by a Koch Weeks conjunctivitis. The usual interval which elapses between the onset of an acute muco-purulent conjunctivitis and the first definite clinical signs of trachoma varies from 6-12 weeks. The virus of trachoma is carried across from eye to eye by flies at the same time as the acute bacterial infection. Fingers are not important in dissemination (but compare SCHNEIDER, above). The influence of climate temperature altitude geographical distribution dust racial predisposition and the like is in no way causal but merely concomitant. Bad hygienic conditions are also only predisposing factors. If the fly scourge in Egypt could be controlled effectively there would be a spectacular and immediate radical change in the incidence of trachoma and acute ophthalmia alike.

Egyptians suffering from trachoma react very differently from Europeans for the tendency towards spontaneous cure is much more evident among the former. This is due probably to a relative degree of inherited immunity rather than to attenuation of virus. The contagiousness of trachoma is not nearly so high as it has always been considered to be except perhaps in the earliest stages when there is a certain amount of active secretion from the eyes. The superposition of an acute or chronic bacterial infection which thus produces an increased quantity of infective material available for the dissemination of the disease is the factor which most enhances the contagiousness of the disease.

Formerly T 1 follicles were regarded as the principal pathognomonic sign of trachoma, but more recent research has proved that there are certain other signs just as pathognomonic. These are not to be looked for in the palpebral conjunctiva, but on the globe. From the 5th-7th day after infection, during the incipient stage of the disease a narrow band of raised limbal oedema, skirting the upper half of the cornea and tailing away in the lower half gradually makes its appearance. It is due to commencing infection of this part of the eye for examination with a corneal loupe or a slit lamp inspection of the limbus shows all the characteristic signs of superficial corneal invasion i.e. engorgement of limbal vessels superficial limbal corneal infiltrations extension of the end capillary loops into the cornea etc. Very soon after the cornea begins to show definite signs of invasion this limbal band of oedema becomes obscured as the mild oedema becomes more generalized.

In the differential diagnosis of follicular conjunctivitis and chronic conjunctivitis from trachoma the absence of invasive signs in the limbus is a certain proof that the disease is not trachoma and if the condition is of short duration an epithelial scraping is of considerable value for inclusions can almost certainly be found if the disease is trachomatous. If one of these diseases is superimposed upon an old trachoma, then it may be impossible to decide upon the true condition. Under the circumstances it is always rational to treat the element of mixed infection first.

Prophylaxis against trachoma in Egypt has been disappointing and so far has only been of benefit in delaying the onset of the disease a little for many



years to come little amelioration can be expected unless some epoch-making medicament is discovered which will effectively control and prevent the disease. The sulphonamides (sulphapyridine, sulphathiazole and sulphadiazine) have proved disappointing in the treatment of trachoma, but, on the other hand, these drugs have proved so highly and so rapidly effective in the treatment of the acute ophthalmias that provided they are given early it is within the bounds of possibility that they may be capable not only of controlling the regular seasonal epidemics of these acute diseases but also indirectly of reducing very considerably the incidence of trachoma at the same time.

The aetiology of trachoma is also discussed by Bland. At present only two theories are generally accepted, the virus theory and the rickettsial theory. The conflict is indeed one of nomenclature rather than of fact and largely depends upon what we choose to call a rickettsia, and what we call a virus. The evidence so far accumulated leads to the conclusion that trachoma is a specific infectious disease not caused by any culturable bacterium, but due to a filter-passing agent which is identical with the elementary and initial forms found in the inclusion bodies (Prowazek-Halberstaedter inclusions) and bearing a close natural relationship to the viruses of inclusion conjunctivitis, lymphogranuloma inguinale and psittacosis. There is no evidence that this agent possesses an arthropod host nor that the louse is the vector of the disease, though the agent may survive for some days in the body of the louse. Bland considers that these four agents stand in an intermediate position between the rickettsiae and the large viruses, and may possibly form a biological link between them. For the present he would prefer to group them with the viruses but to give them a distinctive position as the "basophilic viruses" on account of the blue staining of their initial bodies and of the matrix of their inclusions which distinguish them from the larger typical viruses which do not possess blue initial bodies and whose inclusions are acidophilic.

The bacteriological and clinical observations on the treatment of the acute ophthalmias of Egypt (i.e. those due to the Koch-Weeks bacillus and the gonococcus) with sulphonamides and penicillin are discussed by BLAND and WILSON.<sup>5</sup> The untreated case of acute ophthalmia discharges living and virulent organisms from the eyes for at least 8 days, during the whole of which period the patient is a source of infection for others. By sulphonamide treatment, this period can be reduced to perhaps 1 or 2 days for any case will be rendered non-infective 12 hours after the first administration of the drug and after 2 doses of the drug in every case the conjunctival discharge will be bacteriologically negative for at least the whole of the day following the 2 doses, even in the cases that relapse.

The authors found that sulphapyridine, sulphathiazole and sulphadiazine are all efficacious but as sulphadiazine is the least toxic it is likely to be the drug of choice. The calculation of dosage according to body weight is not always convenient or practical, and they suggest a dosage based on age the following figures serving as a guide (one tablet contains half a gm.) —

0-3 months	1	tablet twice daily
3-6	1	" "
6-12	1	" "
1 year	1	" "
3 years	1	" "
6	1	" "
10	1½	" "
20	2	" "

BLAND J. O. W. & WILSON R. P. Bacteriological and Clinical Observations on the Treatment of the Acute Ophthalmias of Egypt with Sulphonamides and Penicillin. 14th Rep. Memorial Ophthalmic Laboratory Case Cases for 1939-1944 49-71 (70 refs.)

The best way in which to give the drug is to suspend the dose in 2-3 cc of milk and drop it into the child's mouth with an eye dropper. An alternative is to make the dose up into a paste with milk or water and to insert it into the child's mouth on the end of a finger. The authors consider that penicillin is quite unsuitable for the treatment of the acute ophthalmias certainly in Egypt if administered intramuscularly in the form of eye drops for it would impose an enormous strain on the nursing staff and furthermore the Koch-Weeks bacillus is not sensitive to penicillin. Acute ophthalmia is the cause of 80 per cent of the blindness of Egypt and leaves behind in addition a multitude of more or less serious ocular defects. The increased ocular secretion caused by the disease promotes also the spread of trachoma, that second universal plague of Egypt itself a fertile source of damaged sight. No treatment which requires hospitalization or even attendance at hospital no treatment which cannot be taken to the villages where the great majority of the people live and there simply and easily administered can hope to do more than scratch the surface of this problem. The treatment with sulphonamides completely satisfies the conditions. It is simple safe effective and could be given by unqualified persons with a minimum of training it provides the necessary solution not only for Egypt but also for other tropical countries where similar conditions of life and disease prevail.

*Phlyctenular Ophthalmia in Adults* is reviewed by SHAH<sup>6</sup>. A series of 484 cases were examined in the eye out patient department of St Mary's Hospital Lahore. Of these patients 138 (28.9 per cent) were over 20 years of age. In this series males comprised 66.6 per cent and females 33.3 per cent. This is at variance with the widely-held view that the disease is one of childhood and early adolescence and that girls are more affected than boys. Apart from these variations in the age and sex distribution there does not appear to be any other significant difference in the clinical signs and symptoms between the disease in adults and in children. The author's findings agree with those of WANG in Shanghai.

*Epidemic Kerato-conjunctivitis associated with Skin Lesions* is discussed by O'DONOVAN and MICHAELSON<sup>7</sup>. 33 cases were seen. In all cases the scalp or face was affected and there was a strong tendency for the skin and eye lesions to be ipsilateral. In the majority the onset of the skin lesion preceded that of the ocular lesion by a definite but short interval of time. It would appear that lesions of the face and scalp especially those of a seborrhoeic nature may be conducive in some patients to the development of a kerato-conjunctivitis identical with the virus kerato-conjunctivitis occurring in epidemic form. The kerato-conjunctivitis in patients with lesions of the skin is rather more intense as indicated by the greater number with bilateral involvement, adenopathy and deep corneal spread as well as by the slightly longer duration. It is possible that the virus of epidemic kerato-conjunctivitis can possess dermatotropic qualities as do the viruses of herpes simplex and herpes zoster. In this case the lesions of the skin may be considered to be analogous to those found in the skin of patients suffering from herpes simplex and herpes zoster.

*Penicillin in the Treatment of Common External Eye Infections* in out-patients is described by MINTON<sup>8</sup>. The clinical results in blepharitis, conjunctivitis lachrymal sac infections and industrial eye injuries are excellent. Penicillin

<sup>6</sup>SHAH, M. A. A Note on Phlyctenular Ophthalmia in Adults. *Indian Med. Gaz.* 1946, Jan., v 81 No 1 20-22.

<sup>7</sup>O'DONOVAN W. J. & MICHAELSON I. C. Epidemic Kerato-Conjunctivitis associated with Skin Lesions. *Brit. J. Ophthalmol.* 1948 Apr v 30 No 4 183-204 12 figs (including 3 in colour & 5 others on pls.)

<sup>8</sup>MINTON J. Penicillin in Treatment of Common External Eye Infections. *Brit. Med. J.* 1946 Sept. 7 324-8, 1 graph. [19 refs.]

is prescribed in the form of eye drops and ointment. He advocates the following method of preparation of penicillin eye drops. These contain 1,000 or 2,000 units per ml. in sterilized distilled water. Twenty ml. of distilled water are poured into bottles fitted with bakelite caps and rubber washers and then autoclaved at 10 lb (4.5 kgm.) pressure for half an hour. When penicillin drops are required two or four tablets of sodium penicillin (B & W) according to the strength required are added to each 20 ml. The tablets supplied are of three different strengths—0,500 10,000 and 10,500 units per tablet. The method of preparation of the ointment is as follows—it is prepared in the strength of 400 units per gramme. 200,000 units of penicillin in powder form are rubbed in a sterile mortar with a little sterile liquid paraffin. 500 gm. of eucem L31 base (previously sterilized by heating in a sterotherm at 150°C.) are gradually incorporated. The ointment is transferred to sterile jars by means of a sterile spatula.

A biological assay of the penicillin eye-drops proved that the content of penicillin when the eye-drops were kept at room temperature, and the bottles frequently opened and exposed to air was 80 per cent. of its original potency at the end of fourteen days. The penicillin ointment was prepared without water and its stability probably lasts longer than six weeks. The drops and ointment have an ideal pH value for ophthalmic use and are therefore not irritating to the eyes. A number of adults, after using penicillin drops or ointment showed allergic skin reactions of the lids and the skin of the face. These cleared up in a few days when penicillin was stopped.

The use of Penicillin in Ophthalmology is also reviewed by PITTAR\*. He points out that its application is strictly limited and its main use is only in superficial infections of the eye by local application, i.e. for conjunctivitis, corneal ulceration and blepharitis. It may also be found to have a great field in local prophylaxis, in preventing infection following corneal injuries in miners and industrial workers generally and it may practically abolish infection following intraocular operations. For local application he advocates drops with a concentration of 2,500 units per cc. frequency of application is essential. Clarification is needed regarding the use of penicillin in ointment form and in lamellae. Injections of penicillin into the anterior chamber and vitreous are probably only justified in desperate cases. For intraocular infection there seems to be a considerable field for the use of subconjunctival injection and there appears to be fairly good tolerance to daily injections of 500 units in 0.5 cc. of water. The various methods suggested such as corneal bath, ionization injections into the anterior chamber and vitreous all have special disadvantages.

[See also abstracts by DAKIUS and JOHNSTONE in this section below.]

**Malaria**—The ocular complications of malaria are reviewed by GRANT<sup>12</sup>. Opinions on the frequency of ocular complications in malaria have been divergent, depending considerably on variations in the definition of the term "complication" used by the different observers, as well as on the type of disease and thoroughness of examination. In some instances "complication" has been used to signify little more than coincidence whilst in others the term has been restricted to those ocular lesions which could be identified as local effects of the plasmodia.

On inspection of the figures available for the incidence of ocular complications from the standpoint of changes in the eyes which may occur as the result of the development of acute or marked malaria in otherwise healthy subjects, it

\*PITTAR, C. A. The Use of Penicillin in Ophthalmology. *New Zealand Med J* 1946 June, v 43, no. 247 231-5.

<sup>12</sup>GRANT, W. M. Ocular Complications of Malaria. *Arch Ophthalmology* 1946 Jan., v 33, no. 1 45-64. [57 refs.]

appears that the values of 10 per cent (POUCET 1878) and 20 per cent. (SALTZ 1890) which applied to a selection of chronically and seriously ill patients might be excessive whereas the opinion of ELLIOT (1920) that ocular manifestations were rare in India, was influenced by a reluctance to consider as a complication of malaria any ocular disease unless it could be demonstrated to be caused directly by the plasmodium.

DEDINOS (1932) working in Macedonia, stated that the incidence of ocular complication was between 10 and 20 per cent. CARLOTTI (1918) in Greece gave the figure of nearly 10 per cent. FIALHO (1927) in Brazil reported an incidence of 15 to 20 per cent. TOULANT (1938) in Algiers concluded that ocular complications were relatively infrequent. Accounts of experience with ocular complications in World War II by TALBOT (1943) and ROBERTSON (1944) give the impression that ocular manifestations are relatively frequent although no actual figures are given.

Most observers agree that dendritic or herpetic keratitis is the most frequent ocular complication of malaria. Much less often interstitial keratitis has been noted. The keratitis usually occurs in one eye only and its onset is marked by discomfort, photophobia and lachrymation. The cornea is hyperaesthetic, and the lesion stains with fluorescein in the typical dendritic pattern characteristic of the herpes simplex virus in the corneal epithelium. Interstitial keratitis is associated with clouding of the stroma but without vascularization and severe forms have been described as keratitis profunda and disciform keratitis.

Haemorrhages in the ocular fundus have been noted by many observers. Small multiple retinal haemorrhages are usually located in the periphery of the retina and visual disturbances are therefore not observed. The haemorrhages are readily re-absorbed and rarely lead to retinitis proliferans. Large retinal haemorrhages are usually central and temporarily destroy central vision. They are much less common than the small haemorrhages and are limited to malaria with severe anaemia.

The ocular neurological lesions of most significance so far as they affect vision are those of the retina and optic nerve or of the pathways of the brain. The common manifestations are scotomas or loss of vision lasting from a few minutes to several hours followed by severe headache and persistently diminished visual acuity. Dizziness, orbital pain and tenderness with photophobia occur. Changes in the optic nerve and in the fundus sufficient to account for the amblyopia and amaurosis have been described in some cases while cerebral lesions have been considered responsible for the disturbances in others. Those lesions resulting in loss of vision which are evident ophthalmoscopically are optic neuritis or atrophy of the optic nerve and degenerative or haemorrhagic lesions of the retina and choroid. Opacities in the vitreous, iritis and cyclitis are rarely reported except possibly for a mild iritis which occasionally accompanies herpetic keratitis. Cataract is also a rare complication. In the consideration of the usual disturbance in malaria the possibility of toxic effects of quinine in therapeutic use must be ruled out. The changes associated with toxic amblyopia or amaurosis due to quinine are sufficiently typical to be distinguished from malarial manifestations. Amblyopia and blindness due either to minute or massive doses of quinine are rare. At present the mode of toxic action of quinine on the retina is controversial and centres on the question whether the effects of the drug are a result of ischaemia due to alterations produced in the vessels or of a direct toxic action on the neural elements themselves but recent opinion seems to favour a direct action of quinine on the neural elements of the retina as a primary factor.

Relatively infrequently transient ocular motor disturbances, seldom with permanent paralysis have been ascribed to malaria. Of these paresis of the abducens nerve and facial paralysis with lagophthalmos have been reported.

Treatment of these ocular disturbances with anti-malarial drugs has in general been successful, except in the case of herpetic keratitis, caused by a virus for which specific chemotherapy is lacking.

The ocular manifestations in malaria are also discussed by BHATTACHARYA and GUHA<sup>11</sup>. In the conjunctiva, marked pallor may be noted in malarial haemolytic anaemia, and icteric discoloration in the bilious remittent type. In the cornea herpes simplex keratitis varying from mild forms to dendritic ulcers is found in protracted cases of the illness, more often in the convalescent or in the relapsing stages. In the vitreous and retina, haemorrhages have been noticed in a few cases. In rare cases thrombosis of the retinal veins, diffuse retinitis or retinitis proliferans as a sequel to retinal haemorrhages may be produced resulting in permanent impairment of vision. In the neurogenic lesions swelling of the optic disk from 1 to 2 dioptres has been noticed in a number of cases with meningitis and coma. In severe cases papilloedema, with exudates and haemorrhages was seen with dilated pupils and sluggish or absent light reaction. The malarial amblyopia seen was transitory in nature without any fundus changes.

Inequality of the pupils, convergent strabismus and nystagmus were also seen. The authors state that quinine amblyopia or amaurosis are not infrequent complications and that retinal and vitreous haemorrhages may occur after large doses of quinine in persons with a haemorrhagic diathesis and may accompany cutaneous intestinal or urinary haemorrhages.

**Scrub Typhus**—The ocular changes amongst 431 patients suffering from scrub typhus are discussed by SCHIEF<sup>12</sup>. The following external changes were seen: conjunctival hyperaemia occurred in 33 per cent of cases but disappeared during the second and third weeks of the disease; subconjunctival haemorrhages occurred in 6.6 per cent. The haemorrhages were massive, often covering one-third to one-half of the exposed sclera, and were usually bilateral. Echy-mosis of the eyelids occurred in 1 per cent of cases. An eschar typical of the primary lesion of the disease resulting from a mite bite, was seen involving the upper lids in 0.5 per cent of cases. A coarse irregular jerky incoordinate type of nystagmus, occurring only when fixation on an object was attempted, was seen in 0.5 per cent. The following intra-ocular changes were observed. Venous engorgement was the most consistent change in the fundus and always preceded any of the other intraocular changes. It occurred in 67.2 per cent of the patients, with onset during the first or second week, frequently progressing until the veins were  $3\frac{1}{2}$  times the diameter of the arteries. Accompanying the engorgement were irregularity in calibre of the veins and increased tortuosity of the vessels. Oedema of the optic disk and retina was seen in 36.1 per cent of cases. These were always both involved and the condition was always bilateral. In some cases, the swelling of the disk was marked and resembled papilloedema. Retinal haemorrhages, usually superficial, were found in 8.6 per cent of the patients. Fluffy white exudates occurred in 4.9 per cent. These were usually of the cotton wool variety though some resembled gangliform degeneration. The haemorrhages and exudates usually occurred in patients who also had oedema of the retina and disk. Dust like vitreous opacities most numerous in the posterior vitreous without further evidence of uveitis, were seen in 4.6 per cent and definite uveitis in 1.3 per cent of the patients. The uveitis was usually indolent in character with slight photophobia and usually without ciliary injection. It was nearly always associated with oedema of the

<sup>11</sup>BHATTACHARYA, B. P. & GUHA, G. S. Ocular Manifestations in Malaria. *Indian Med. Gaz.* 1946, Feb. v. 81, No. 2, 79-80.

<sup>12</sup>SCHIEF, H. G. Ocular Changes in Scrub Typhus. A Study of 431 Patients. *Bull. U.S. Army Med. Dept.* 1946, Apr., v. 3, No. 4, 423-7. 4 figs.

disk and retina. Visual acuity was undisturbed except in patients with uveitis who occasionally complained of blurred vision. From the pathological investigations available it would appear that the primary lesion in the eye consists of an inflammation of the highly vascular uveal tract. This might be expected for one of the characteristic pathological changes of scrub typhus is a vasculitis and perivasculitis of the smaller blood vessels. The incidence of vitreous opacities and bilateral uveitis supports such pathological findings. Even though the clinical picture suggests a retinopathy, the disturbance in the choroid is probably the underlying factor.

*Visual Defects in Prisoners-of-War from the Far East* are described by HOBBS & FORBES.<sup>12</sup> More than 2,500 men liberated from Japanese prisoner of war camps were seen. Defects of vision recovered or still present were a prominent feature of the history. They were classified into three broad groups—

Group I—defective reading vision only, usually, transient.

Group II—transient blurring of both reading and distance vision.

Group III—a persistent defect of both reading and distance vision.

Patients in groups I and II mainly presented problems of refraction and appeared to have had a temporary asthenopia associated with their very debilitated condition before liberation. The visual acuity was within normal limits, and no abnormalities of media, fundi or ocular movements were seen. Group III numbered about 250 persons and comprised a few men with active ocular disease, a number with fully correctible refractive errors in whose visual fields no scotomata appeared, and a larger group in whom correction with lenses produced little or no improvement and whose visual fields showed absolute or relative scotomata to white test objects. These cases form a group of 163 cases of partial optic atrophy. The history of 89 per cent of these 163 cases was of gradual deterioration of vision after the first or second year of captivity, occurring as a general blurring of vision or as scotomata. The visual loss increases over a period of weeks or months, but a rapid onset was not uncommon and in 11 per cent, the visual loss had developed within twenty-four hours. In many cases the onset was insidious and unrelated to other disease. In regard to refraction 6 per cent had visual acuity of less than 6/60, 55 per cent, had visual acuity between 6/60 and 6/24, 33 per cent, though subnormal were better than this, and 6 per cent had 6/6 in both eyes.

Pallor of the central halves of the disks was present in most cases. Signs of retinal disturbances were not common and when present were noted between the macula and the disk. Perimetry showed no significant constriction of the peripheral fields in any except the more severely affected cases. Examination of the central fields revealed various types of defects, all of which lay in the centro-caecal area. The most common finding was bilateral absolute central scotomata to 2, 5, 10 or 15/2,000 white, and in such cases the associated loss of visual acuity was correspondingly great. In others less severely affected, scotomata less dense and less centrally placed appeared, and these often took the form of central and paracentral relative scotomata, with eccentric absolute nuclei, which in some cases formed a partial ring and left the fixation area clear. In others there were minute scotomata about the central area, where the 2 mm. white object appeared to flash on and off.

Group III cases, showing scotomata and partial optic atrophy, were closely related to preceding infection, particularly malaria and dysentery. In the former an increased metabolism and in the latter decreased absorption from the diseased intestine producing a greater lack of those factors which normally prevent the development of this syndrome.

<sup>12</sup>HOBBS, H. E. & FORBES, F. A. *Visual Defects in Prisoners-of-War from the Far East.* *Lancet* 1946 Aug 3 149-53 5 figs. [15 refs.]

The response to treatment was poor. The superiority of animal protein over yeast in prevention and treatment suggests that some factor besides Vitamin B contained in animal protein, is necessary to prevent the onset of these lesions, and that the lack of protein is a precipitating factor in the disease. It may well be that the rôle of protein consists in promoting the biosynthesis of vitamins in the intestine.

*Nutritional Retrobulbar Neuritis* or nutritional optic neuropathy, is reviewed by MOORE<sup>14</sup>. The aetiology is still far from complete. He is of opinion that it can be excluded from beriberi though it can be associated with it. The response of the visual condition to autoclaved yeast and the investigations with thiamin in the prisoner-of-war camps, are impressive evidence against beriberi. In West Africa nearly all cases were either accompanied or preceded by hyporiboflavinosis, but it would not be safe to state that riboflavin deficiency caused the neural condition for trials with riboflavin have never been sufficiently extended. Lack of riboflavin is no doubt an important causal factor but other vitamins of the B complex excluding thiamin may also share in the cause. The same is partly true for nicotinic acid, though there is more evidence that lack of this vitamin is not directly concerned. Experiences in prisoner-of-war camps appear also to support this view. Treatment has yielded important results provided it is begun early, the dosage (marmite or brewer's yeast) is high and it is maintained over a long period.

The clinical features are important for there are distinct variations and superimposed conditions to be found. Keratitis was rare in Nigeria, but common in Sierra Leone and apparently in prisoner-of-war camps. The Jamaican cases were fulminating. Beriberi is rare in Nigeria, but common among ships' crews, on a diet of rice and salt fish from Sierra Leone and Liberia. In Nigeria, retrobulbar neuritis was extremely common but in certain areas only or under bad conditions which existed in some schools before the war. It was not seen in those areas where yams or sweet potatoes or better class cereals, formed the staple carbohydrate. As early as 1933 the author was convinced that manioc was the dietetic cause for the disease was essentially confined to the manioc eaters. But in Jamaica manioc was replaced by sugar cane in Sierra Leone and Spain (civil war conditions) largely by rice and in China and the Far East solely by rice. Where the rice was unpolished or as in prisoner-of-war camps reinforced with barley and soya bean there was least evidence of retrobulbar neuritis. A theory based on an exogenous toxin therefore can only be upheld if it can be proved to be common to all conditions. There is an obvious alternative explanation—a theory based on an endogenous breakdown. It may be that certain foodstuffs do possess inhibitory toxic factors and also help to accelerate metabolic breakdown (e.g. cyanogenetic factors—alcohol in secondary pellagra).

What has been established is that under conditions of duress or environmental restrictions, leading to an insufficiency in normal intake of protein (and, to satisfy hunger a relative over-consumption of energy foodstuffs poor not merely in vitamin B<sub>1</sub> but in all the B vitamins) nutritional retrobulbar neuritis has been common. Other syndromes such as beriberi may of course co-exist. Why say that rice can cause only beriberi, when it is poor in all nutrients? Where there is a gross dietary imbalance and where cereals of poor quality are almost the sole source of energy and protein is deficient then we can be certain that this visual complaint and the associated primary deficiency status must remain. It is not enough to ensure an adequate crop of rice or manioc—we must also aim at a vast improvement in the variety of carbohydrate foods and in the diet as a whole and a rise in the economic standards of life.

<sup>14</sup>MOORE, D. F. Nutritional Retrobulbar Neuritis. Nutritional Optic Neuropathy. *Lancet*, 1946, Aug. 17, 46-8, 3 figs. [33 refs.]

**Nutritional Optic Neuropathy.**—The syndrome of epithelial and nervous lesions complicated by nutritional optic neuropathy is reviewed by WRIGHT<sup>15</sup> He found defective vision to be a cause of constant complaint and attributed its origin to deficiency of vitamins A and B. He therefore introduced in 1927 the active treatment with yeast and cod liver oil. In Sierra Leone the dietary is deficient in protein and hence in sulphur. In 1936 he described the experimental treatment of the syndrome with organic sulphur using Contra mine parenterally in some cases and ichthyol orally in others. Judicious sulphur therapy was of great benefit to the patient and resulted in economy in treatment. Although good clinical results have consistently been obtained by combined sulphur and vitamin therapy in Sierra Leone he has seen no record of its use in nutritional optic neuropathy.

**The Nature of Starvation Amblyopia** in 277 cases in Camp Nakom Paton is analysed by HAZELTON.<sup>16</sup> The aetiology of the disease seems to be bound up with a combination of vitamin deficiencies. The disease resolves itself into two parts. (1) Easy exhaustion of the ciliary muscles which is cured by the administration of sufficient doses of thiamin at least 1 000 international units intramuscularly each day for 14 days. Also the symptoms of eye strain (pain in the eyeballs frontal headaches, excess lachrymation heaviness of the lids and tired feeling of the eyes which increased after reading) were alleviated by the administration of thiamin. (2) A condition of degeneration of the cones of the retina which itself is probably brought about by the lack of sufficient photo-sensitive substance for these receptors. The former is shown (a) by lowering of the visual acuity (b) inability to differentiate objects close together (c) interference with colour vision. The latter is postulated from the fact that the colour of print appears to change on reading from black to green or yellow. Two facts emerge from this —

1. There is a definite relation between eyestrain and vitamin B<sub>1</sub> deficiency.

2. Sufferers from avitophthalmia are liable to sustain further damage to their cones in bright light. They should not work in sunlight and should wear dark glasses. Any degeneration of the retina is probably permanent and in early cases every effort should be made to supply a well-balanced diet failing the elucidation of the specific factor causing the disease. The results of treating cases of nutritional amblyopia of short duration with 10 eggs per day for thirty days were very gratifying. All cases undergoing this treatment showed a distinct improvement.

**The Ocular Symptoms and Signs associated with Deficiency of Vitamin B Complex** are discussed by FERNANDO AYUYAO and CRUZ.<sup>17</sup> Their report is based on the observations of 590 adult patients in the Philippines and is the first epidemic of this nature ever reported in that country. The chief complaint was dimness of vision in both eyes the cause of which was (1) chronic retrobulbar neuritis (2) superficial vascularizing keratitis or (3) both affections co-existing. The patient invariably gave the history of having subsisted for some time on a diet very deficient both in quantity and in quality. They were healthy up to the time of onset of their complaint. Adult males and females were attacked. In females pregnancy and lactation were predisposing factors. In many patients associated signs and symptoms of vitamin B complex deficiency were observed namely angular stomatitis glossitis numbness around the mouth hyperaesthesia or hypoaesthesia in the extremities and other manifestations.

<sup>15</sup>WRIGHT E. J. Nutritional Optic Neuropathy [Correspondence.] *Lancet* 1946 Sept. 14 401-2.

<sup>16</sup>HAZELTON A. R. The Nature of Starvation Amblyopia. *J. Roy. Army Med. Corps* 1946 Apr. v 86 No. 4 171-8.

<sup>17</sup>FERNANDO A. S. AYUYAO C. D. & CRUZ J. N. Ocular Symptoms and Signs associated with Deficiency of Vitamin B Complex. *J. Philippine Med. Ass.* 1946, Mar., v 22, No. 3 93-107 [14 refs.]



EL TONGY A. F. A Scheme for Massive Abortive Treatment of Acute Ophthalmias by Chemotherapy. *14th Rep Memorial Ophthalmic Laboratory Giza Cairo for 1939-1944* 107-17

NASHEED E. Chemotherapy of the Acute Ophthalmias. *14th Rep Memorial Ophthalmic Laboratory Giza Cairo for 1939-1944* 129-32.

FAMILIARI, P. La cecità acquisita tra gli indigeni dell'A.O. problema clinico e sociale. [Acquired Blindness in the Natives of East Africa—a Clinical and Social Problem.] *Boll Soc Ital di Med e Igiena Trop (Ser. Eritrea)* 1945 v 5 Nos 5/8, 85-89. English summary (7 lines)

BLAND J. O. W. Spontaneous Folliculosis of the Conjunctiva in Baboons (*Papio hamadryas*). *14th Rep Memorial Ophthalmic Laboratory Giza Cairo for 1939-1944* 87-8

BLAND J. O. W. Spontaneous Folliculosis of the Conjunctiva in Grivet and Vervet Monkeys (*Lanopys gracioridis* Syn. *Cercopithecus aethiops* and *L. pygerythra* Syn. *C. pygerythra*) and the Susceptibility of the Grivet to Trachoma Virus. *14th Rep Memorial Ophthalmic Laboratory Giza Cairo for 1939-1944* 72-86. [16 refs]

#### CORRESPONDENCE.

In the abstract of the paper by BENENASOONT on trachoma [this *Bulletin* 1945 v 42, 488] the statement is made that the author treated a small number of incipient cases of trachoma with a preparation containing vitamins A and D by the mouth, without local applications. The author points out that 24 cases were treated, of which 9 were incipient and 15 in the granulomatous stage (2 having complications). The results were good. He also remarks that cod liver oil has been used with good effect as the source of vitamins A and D—Ed

#### TROPICAL ULCER.

L. NATH T. Tropical Ulcer in the Hissar District of the Punjab. *Indian Med Gaz.* 1946 Apr-May v 81 Nos 4/5 169

LI. LUTHERA, P. N. Ulcus Tropicum in Fazilka (Punjab) *Ibid* 169-71

1. It is pointed out by the author that whilst tropical ulcer has been reported in the humid climate of Assam and South India, and other parts of the country no cases had been reported so far from the Punjab

The paper discusses 60 cases seen in the Hissar district of the Southern Punjab where rainfall is very low and the soil is mostly sandy

The clinical, aetiological and microscopic features described by the author follow the now well recognized picture. Two points of interest are that most cases occurred under the age of 18 years, and that they were most frequent between September and January

Three groups of 20 patients were subjected to different treatments, namely—(1) scraping, followed by dressings of 5 per cent. copper sulphate (2) scraping and sulphonamide powder and (3) strapping with leukoplast for at least 10 days

The first two groups took about 35 days to heal, whilst the third did remarkably well and healed in 15 days.

The author noted scars on the lower limb in several patients examined for medico-legal identification and presumed therefrom that the ulcer had existed in the district for a number of years.

ii. This author saw 106 cases of tropical ulcer in the out patient department in Fazilka a small town in the Ferozepore district of the Punjab with a population of 26 000. The climate is very hot and dry in summer and cold and dry in winter. The average rainfall is about 10 inches but in 1944 it reached about 16 inches.

The author describes the disease as assuming a mild epidemic form after the unusually heavy rains in 1944 and a milder epidemic was also noticed after the summer rains in 1945. [The use of the word epidemic is perhaps something of an overstatement.]

The description of the cases closely resembles that given by the author quoted in the preceding abstract. Over 50 per cent of the patients were under 16 years of age and 95 per cent were under 30. Only 10 were females.

Twenty-eight hospital patients were treated by complete rest and daily cleansing of the ulcers with a solution containing 3 drachms of copper sulphate, 1 drachm of carbolic acid and 1 ounce of water. The ulcers were then dressed with boro-iodoform. With this treatment the average stay in hospital was 14 days. When half of the patients were treated with dressings of magnesium sulphate and sulphonamide powder in equal parts the average stay in hospital was 20 days. Penicillin dressings used in one case only did not accelerate recovery.

The author's experience that the disease is one affecting the poor and ill nourished agrees with that of the previous author writing from Hissar and indeed with that of most observers and he sounds a note of warning that it may well spread and assume severe epidemic proportions under the serious food conditions now prevailing in India, a danger which health authorities and others should take anticipatory steps to meet.

[Although these papers have little new to add to the large dossier of tropical ulcer, the close resemblance between these independent testimonies in different parts of a Province where tropical ulcer was not believed to occur is significant and there is sound sense and humanity in the timely reminder for the need to take advance account of this additional potential complication of the already severely taxed vitality of the people in the famine-afflicted regions of India.]

H. J. O'D. Burke-Gaffney

GOLDEN A & PADILLA, E. Tropical Ulcer in Guatemala. Pathologie, Bacteriologie, Mycologie and Clinical Aspects. *Arch Pathology* 1946 June v 41 No 6 612-30 3 figs.

This paper represents the results of observations made by the authors on 24 patients suffering from tropical ulcer. All the patients originated in the lowlands—from sea level to 1 000 feet—and were predominantly American Indian and Indian-Caucasian though all types in the lowlands were included Indian, Caucasian and Negro.

The patients comprised members of age-groups from 11 to 56 years of both sexes. Sex and occupation did not appear to affect incidence significantly.

Full histories were obtained and physical and laboratory examinations were made and the investigation included the dietary history of the patients. No common nutritional deficiency was noted.

Routine clinical laboratory tests revealed nothing of new importance and bacteriological examination including attempts to isolate fungi were inconsistent and added nothing to the list of recognized flora.

The authors exclude various causative factors in their series one by one, but place most significance on the biopsy findings. After describing the general

and usually recognized histological features of tropical ulcers they note that the distinguishing feature in all cases was to be found in the vascular changes. These consisted essentially of thickening and narrowing of the lumina of vessels which were occasionally obliterated and sometimes recanalized. These signs were found, to some extent, alike in arteries, veins and capillaries.

Detailed descriptions of these histological changes are given and the authors believe that they are primary vascular changes and not secondary to inflammation. Arguments are given in support of this thesis the chief of which are that (1) even the most severe vascular lesions were found in all cases at an early stage (2) the most pronounced vascular changes were situated away from the zones of greatest inflammatory exudate (3) the condition is entirely different from the endarteritis or vasculitis commonly encountered as secondary to inflammation.

In the absence of any other specific factors, the authors consider that the vascular feature stands out clearly for it was common to all cases. They discuss the possible causes of these vascular changes but were unable to find any one specific reason for the interference with local blood supply. They consider that treatment of tropical ulcer should aim especially at restoring the adequacy of the blood supply to the part.

[Among the vast number of factors which have been indited as causes of tropical ulcer there have frequently been included that of inadequate blood supply to the affected part. Where the authors further confirmatory study is especially valuable is in the carefully described and well-illustrated histopathological investigations.]

H. J. O'D. Burke-Gaffney

### MISCELLANEOUS DISEASES

- I. MANSON BARR, P. E. C. & CHARTERS, A. D. Epidemic Thrombophlebitis in the East Africa Command. *Lancet* 1946 Sept. 7 833-5 3 figs.
- II. FISHER, A. C. & LENDRUM, A. C. Epidemic Thrombophlebitis [Correspondence.] *Ibid* Sept. 21 438.

I. The authors describe a syndrome of recurrent thrombophlebitis accompanied by pyrexia often relapsing and sometimes associated with stiff neck, among East African soldiers. No previous record of this condition was known to the authors but they quote GELFAND who in his book "The Sick African" refers to the condition of acute thrombophlebitis of unknown aetiology described in N Rhodesia by FISHER [*this Bulletin* 1942, v 39 199].

Occasional cases had been seen in the East African Command during 1941-1943 but in 1944 the disease began to assume epidemic proportions and cases were observed independently at three different centres most, but not all, of the 627 patients with this syndrome, admitted to two General Hospitals had previously been treated for venereal disease at special centres.

The authors describe the clinical features observed in 145 cases three varieties of the syndrome were seen —(1) a short term fever with stiff neck often followed by relapses (2) thrombophlebitis affecting one or more limbs, tending to relapse (3) pyrexia, usually relapsing without evident phlebitis. As stated above most of these patients had received treatment for venereal disease, which involved venepuncture but 23 did not give a history of injection. The interval between the last injection and the onset of symptoms varied from three days to seven months. The first variety short-term fever with stiff neck, developed either as the first phase of the syndrome or as a sequel to previous attacks of phlebitis it lasted 2-30 days, usually about 4 it usually relapsed,

with stiff neck or thrombophlebitis but occasionally without either. There was no sign of cervical thrombophlebitis. Laboratory examinations including some attempts at bacteriological culture were negative, except for relative lymphocytosis in a few cases. The second variety thrombophlebitis affecting one or more limbs was either acute or subacute in most cases but a chronic form, a form with involvement of the portal vein and a form associated with arteritis are described. Again laboratory investigations were negative and biopsy of the affected vein in 6 cases showed simple thrombosis only with no evidence of inflammation of the wall of the vein. The veins of the legs were most commonly affected but in 20 of 105 cases the veins of the arm were thrombosed. In no case was embolism noted.

In the third variety the pyrexia was irregular and lasted for 3-21 days without evident phlebitis; in many of these cases the diagnosis was suggested by a history of recent anti-syphilitic therapy.

The authors discuss the differential diagnosis of these conditions.

The cause of this disease is still unknown. That it may be due to a virus possibly transmitted during intravenous medication for syphilis, is suggested by the relative lymphocytosis, the negative bacteriological findings and the fact that the curve of incidence followed quite closely the curve of incidence of hepatitis which was related to administration of arsphenamine. No antibodies to Rift Valley fever were found in two patients examined. It is possible that the administration of arsenic or bismuth predisposed to the present syndrome, perhaps by rendering the veins susceptible to infection. There was no evidence that this thrombophlebitis was related to marasmus—most of the patients were well nourished. The authors note that thrombophlebitis is not common in the civilian Africans of the area.

11. In this letter Fisher and Lendrum refer to the pathological findings in the veins in the Northern Rhodesia cases mentioned above.

It has come to be appreciated (A.C.F.) that only a short stretch of the vein was primarily involved and microscopy of this zone has now revealed a peculiar form of inflammation characterised by extreme proliferation of young capillaries in the disrupted media of the vein and by the presence of phloxinophil intracytoplasmic inclusions.

Charles Wilcocks

JACOBY H. Curative Treatment of Lathyrism, a Disease of the Nervous System. *Indian Med Gaz* 1946 v 81 Nos. 6/7 248-7

The author reports favourably on prostigmine.

COX C D & ARBOGAST J L. Melioidosis. *Amer J Clin Path* 1945 Dec v 15 No 12 567-70 [14 refs]

This paper reports a case of melioidosis in a 27 year-old American infantry man who died on the 8th day of disease. He had been 21 months overseas 20 of which had been spent in Burma the month preceding admission to hospital he had been located at Dujana in Assam. Illness started acutely. There was a swinging temperature up to 105°F. Liver and spleen were both palpable and scattered pustules appeared over the entire body. Clinical diagnosis was one of generalized septicæmia of undetermined aetiology. Post mortem abscesses averaging 0.8 cm. in diameter were present in the skin, liver, spleen, lungs, lymph nodes, epididymis and testicle. They were most numerous in the lungs where they were becoming confluent. Histologically they were characterized by a central zone of coagulation necrosis surrounded by a haemorrhagic zone, numerous polymorphonuclear leucocytes were

present. A motile Gram-negative bacillus, isolated from the blood and skin lesions during life and from the lesions post-mortem, was identified as *Malleomyces pseudomallei* (Pf) Whitmore.)

S. P. Bidson

ASHLEY, P. External Otitis in the Tropics. *U.S. Nav. Med. Bull.* 1946 Aug v 46 No 8 1230-36 4 figs.

Ashley states that the cases of external otitis which occur in ships operating in tropical waters may be divided into three categories.

In the first group the men complain of pain in the ear discharge, partial deafness itching or burning. The auditory canal is partly or wholly blocked with a cheesy or flaky mass consisting of cellular debris and moist exudate, in which purulent matter may occasionally be incorporated. If the meatus is cleaned its walls are found to be raw red and, sometimes, bleeding they may also be slightly oedematous.

Ashley recommends that the ear should be thoroughly cleansed and if X-ray therapy is not available (he regards X rays as the ideal treatment for all forms of external otitis) the meatus should then be swabbed with a 4 per cent. solution of boric acid in 50 per cent. ethyl alcohol. Thereafter a cotton wick impregnated with 10 per cent. aqueous solution of sodium sulphadiazine should be inserted and left in place. This dressing should be changed thrice daily. On the third day if the walls are dry the treatment is changed the toilet of the ear is carried out twice daily and a search is made to determine which of ten preparations—the formulae for which are given—will suit the patient best and complete the cure. The preparations vary from sulphanilamide powder to a lotion containing 1 gramme of benzoic acid, and 1 gramme of salicylic acid in 30 cc. ethyl alcohol. The ten preparations are shown below—

Formula No. 1	Gm. or cc.
Salicylic acid	1.0
Ammoniated mercury	1.0
Rose water ointment	30.0
Mix.	
Formula No. 2	
Ammoniated mercury	1.0
Petrolatum	30.0
Mix.	
Formula No. 3	
Salicylic acid	1.0
Ethyl alcohol 95-per cent. to make solution	30.0
Formula No. 4	
Sulphanilamide powder	
This is best instilled with a powder blower	
Formula No. 5	
Sodium sulfadiazine ointment 5-per cent.	
This is a new item in the Supply Catalogue.	
Formula No. 6	
Sulfathiazole powder	1.5
Petrolatum q.s. ft.	30.0
Mix.	
Formula No. 7	
Salicylic acid	3.0
Ethyl alcohol 95-per cent. to make solution	30.0
Formula No. 8	
Thymol	0.6
Cresatin q.s. ft.	30.0
Mix.	

## Formula No. 9

Ichthammol	1 2
Naphthalan	6-0
Zinc oxide	15-0
Starch	15-0
Petrolatum q.s ft	60-0
Mix.	

(This preparation is not available at sea but is very effective in Group 3 cases.)

## Formula No. 10

Benzoic acid	1-0
Salicylic acid	1-0
Ethyl alcohol 95-per cent. to make solution	30-0

Benzoic acid was not available but we feel that this so-called liquid Whit fields would be of use in some cases.

The second variety of otitis externa is more acute. The patient's temperature may be raised to 103°F and the ear is exquisitely tender. The walls of the auditory canal may be oozing or dry but they are very oedematous. This variety of otitis externa responds to rest in bed, oral administrations of sulphadiazine and the application of heat to the ear from a partly filled hot water bottle. After 24 hours the patient is usually so far recovered that he will submit to local therapy. The meatus is then cleansed, and a wick impregnated with metacresyl acetate (cresatin) is inserted and renewed thrice daily. After some 3 or 4 days he may leave his bed, and local therapy continues as for cases of Group I.

The third group consists of patients who complain of itching and occasional slight pain in the ear. The walls of the canal are found to be dry and scaling. The condition may arise *de novo* or may be a sequel to the other types of inflammation described above. Treatment consists in carrying out the toilet of the ear regularly and using one or other of the ten applications which the author has listed for use in cases of Group I.

Ashley believes that the adverse climatic conditions of the tropics associated with the entry of water into the ear whilst the patient is bathing under a shower or swimming and the removal of wax from the ear with toothpicks and other implements, should all be considered as aetiological factors. In cases of Group 3 the production of dry wax or no wax or oil at all in the ear canal leads to scaling and fissuring of the skin giving the picture commonly known as eczema of the external ear canal. Fully developed this eczema is identical with the picture seen in Group 3 and may quickly develop into either of the other two types.

R M B MacKenzie.

KEAN B H & TUCKER, H A. *Etiologic Concepts and Pathologic Aspects of Ainhum. Arch Pathology* 1946 June v 41 No 6 639-44 1 fig [33 refs.] [Refs. in footnotes.]

The authors group the aetiological factors comprising the many theories as to the causation of ainhum under three general headings: infectious, constitutional and mechanical.

In this paper they discuss the literature under these general heads and then describe the records of 45 sufferers from ainhum on the Isthmus of Panama 12 of whom they had observed clinically.

All the patients were negro males and the little toe was the only digit involved. A deep encircling groove separated the toe from the remainder of the tarsus at the level of the digito-plantar fold. In advanced cases the constriction progressed until only a thin pedicle kept the small potato-like toe to the foot.

The histopathological features conformed to the recognized descriptions of ainhum but the authors consider that in published reports undue significance is commonly placed on a number of features and they express the following opinions —

- (1) The groove is not caused by a *constricting band* of fibrous tissue.
- (2) Identical epithelial changes may be seen in the toes of those not suffering from ainhum.
- (3) The vascular changes noted are not specific to ainhum.
- (4) The nerve and gland changes do not appear significant. The authors found it difficult to evaluate the atrophy of bone and the subcutaneous inflammatory reactions, which seemed to be significant but the evidence that the essential lesion of ainhum might be chronic osteomyelitis was not impressive, although the low-grade cellulitis and fibrosis of the corium were more suggestive.

The authors conclude that the cause and pathogenesis of ainhum are not clear but that the racial factor seems most important.

H J O'D Burke-Gaffney

HERSH, J. Ainhum. Report of a Case. *J Internal Colls of Surgeons*. 1946, July-Aug., v 9 No 4 477-81 2 figs

SAXIAL, S. C. Pedunculate (for the Treatment of Bengal Splenomegaly) *Indian Med. Gaz* 1946 June-July v 81 Nos. 6/7 242-3

CAYTON, F. G. Some Risks from New Remedies in Tropical Diseases. Reprinted from *Med Press & Circular* 1946 May 29 361-2.

## GENERAL PROTOZOOLOGY

PLAUT, A. The Problem of Human Toxoplasma Carriers. *Amer J Path* 1946 Mar v 22, No 2 427-31 6 figs. on 1 pl.

In the case of a boy who died of severe jaundice, associated with enlargement of the liver and spleen and ascites and also in the case of a woman who died of peritonitis following operation for intussusception, bodies presumably parasitic in nature were found in the myocardium. In the first case two masses were seen in enlarged muscle-fibres. Each mass, which had a fairly distinct outline consisted of numerous closely-packed particles about  $1\mu$  in diameter. In the second case a single group of somewhat larger radially arranged bodies, each with a central nucleus was seen. In neither case was there evidence of parasitic invasion elsewhere in the body. Slides and photographs were submitted to a number of experts, who failed to agree as to the significance of the structures, suggesting among other things that they were sarcosporidia, toxoplasma or contaminants. The author calls attention to the organisms which are illustrated in photographs because of their importance from the point of view of the discovery of carriers of toxoplasma infection. C M Heycox

## GENERAL ENTOMOLOGY

BEADLE, L. C. An Ecological Survey of some Inland Saline Waters of Algeria. *J Linnean Soc Zoology* 1943 v 41 No. 278 218-42, 1 fig [38 refs.]

This paper is the result of an expedition to study the saline inland waters in Algeria in the winter of 1938. They ranged in density from 1 000 to 1 172

(fresh water=1 000 sea water 1 022) Analyses for the various ions were made pH values alkalinity and other data are given. The fauna and flora found can be divided into three groups —(i) freshwater species only found in low salinities (ii) forms only found in intermediate salinities (iii) forms capable of living in extremely saline waters. Many interesting and useful results of ecological importance are given but few forms of direct medical importance were found. *Aedes detritus* and *Aedes caspius* which are confined to saline waters were recovered several times. *Anopheles multicolor* was found once in stagnant water having a density of 1 008  
*Kerneth Midland*

WOLFF J. Note sur les moustiques de Coquilhatville (Deuxième note) [A Note on the Mosquitoes of Coquilhatville. Second Note.] *Ann Soc Belge de Méd. Trop.* 1946 June 30 v. 26 Nos 1, 2, 95-104 1 fig.

HILL, R. B. & HILL, Claire M. A List of the Mosquitoes found in Jamaica. *Catalogus Insectorum Jamaicaensis Supplement* 1945 3 pp. Dept. of Agriculture Jamaica Kingston Govt Printer

The compilers of this list have made extensive collections of mosquitoes in various parts of Jamaica and in the past three years have found one new species and 13 others hitherto unreported from the Island. Three other species new to Jamaica and found by other workers are included. A total of 50 species is listed and the list includes many mosquitoes of medical importance.  
*H J O D Burke Gaffney*

WANSON M & LEBIED B. Un nouvel Anophèle cavernicole du Congo belge *Anopheles (Myzomyia) rankoofi* spec. nov. [A New Cavernicolous *Anopheles* from the Belgian Congo] Reprinted from *Rev. Zool. Bot.* 1945 Dec 29 v. 39 No. 1 118-29 19 figs.

In the lower part of the Belgian Congo near Thysville there is a very large cave which is known to extend at least a mile from its entrance. It contains a remarkable fauna, including a blind fish, cave crickets and so forth, also two giant species of *Phlebotomus*.

The authors here describe a new species of *Anopheles* from this cave. The early stages have been found in total darkness in a chamber some three hundred yards from the entrance. They occur in small basins in the rock which are filled with water that drips from the roof; the adults are found in the same place and it is thought that they never leave the cave but feed on certain bats (*Myotis*) which are abundant.

The adult mosquito is large and dark without ornamentation on the legs or palps and with only some very obscure pale spots on the wings; there are small differences in the wing markings between the male and female. The morphological characters of the larva and adult indicate clearly that it is a *Myzomyia* and that it probably belongs to the group *Eomyzomyia* with affinities to *A. wilsoni*. [So far as we are aware this is the first record of a completely cavernicolous mosquito.]  
*P A Buxton*

KAUF F W. Improvements in Equipment for killing both Larvae and Adult Mosquitoes with DDT. Reprinted from *Agric. Engineering* St Joseph Michigan. 1945 Nov., v. 26 No. 11 459-62 464-468, 5 figs.

The introduction of DDT involves changes in spraying equipment because the dosages applied and the degree of atomization required differ from those of preparations formerly used.



A hand gun of the Cobra type has been developed which will operate at pressures between  $\frac{1}{2}$  and 1 atmosphere (7-14 lb./sq. in.) The orifice is 1 mm. in diameter and with a working pressure of 0.5 kgm./cm<sup>2</sup> ( $\frac{1}{2}$  atmosphere) this will deliver 2.5 cc. of DDT-oil solution per minute. This permits easy coverage of an acre with one quart of oil. The same type of nozzle can be used without the hand plunger pump by attachment to an independent air supply. The nozzle can be adjusted so that, at 1 atmosphere pressure it will deliver from 2.5 to 110 cc. per minute. Up to 54 cc. an excellent pyrethrum type spray is produced (atomized mist) and just above this a wet spray is formed which is suitable for treating walls.

A small hand operated air-pump has been devised for use with the sprayers. This is operated by a lever in the same way as the ordinary knapsack oil-spray pump. It develops a pressure up to 2 $\frac{1}{2}$  atmospheres. It can either be used in conjunction with a knapsack tank or the air can be delivered to a hand sprayer with a container. Two such pumps strapped on a brace on the back of an operator will supply air for a single spray-gun carried by another operator. This arrangement is convenient for indoor spraying where the sprayer has to be manoeuvred over furniture etc.

Types of spray patterns are discussed. The fan-shaped spray is considered preferable to the round spray for careful treatments in furnished houses. Fan-shaped sprays can be produced by suitable nozzles, both with air-atomized and pressure-atomized (whirling jet) sprays.

A convenient extension arm can be made from 6 mm. aluminium or copper tubing led through bamboo poles drilled lengthwise. An extension of this type four to five metres long is not too heavy and is useful for spraying high barns, etc.

J. R. BURTON

DAVID W. A. L. The Quantity and Distribution of Spray collected by Insects flying through Insecticidal Mists. *Ann. Applied Biol.* 1946 May v 33 No. 2 133-41 2 figs & 1 pl. [12 refs.]

If a housefly or a mosquito (*Aedes aegypti*) flies through a mist of finely divided insecticide droplets accumulated in transit can be seen by subsequently examining the wings. On other parts of the body oil-carried insecticides spread rapidly but by use of an aqueous spray droplets can also be found on the antennae, eyes, mouthparts, large body bristles, the halteres and on fine hairs guarding the anterior spiracles. If a spray mist is produced with oil dyed with Sudan III, and the flies are dissected at intervals after exposure, it is found that the dye penetrates the integument, is extracted from the haemocoel by the Malpighian tubules and excreted through the anus. Houseflies with mouth and anus blocked were found to show large quantities of dye in Malpighian tubules and rectum one hour after spraying.

A colorimetric method is described by which the quantity of spray drops packed up during flight can be estimated. With both *Musca* and *Aedes* about three times as much spray is deposited on the wings as on the body. With insecticides which do not cause paralysis, much of this deposit is removed during the course of twenty-four hours. Deposit on the wings is removed by cleaning movements of the legs and there is also a general absorption and excretion. Penetration of the cuticle does not appear to occur in dead insects.

The quantity of spray accumulated depends on the physical qualities of the mist, especially on the size and number of drops. Much more is accumulated directly after spraying than in an equivalent period with a mist four to ten minutes old. The addition of a small quantity (5 per cent.) of a non-volatile oil reduces evaporation of the droplets, which therefore remain of large size as a consequence, many more impact on flying insects.

By the quantitative method it is possible to estimate the median lethal dose of different insecticides as deposited from spray mists. Thus —

Insecticide	Median lethal dose (mgm. per kgm live weight)			
	<i>Musca</i> (3-5 days old)		<i>Aedes</i> (1-4 days old)	
	Males	Females	Males	Females
DDT (0.3 per cent. sol.)	6.0	9.0	5.5	8.0
Gammexane (0.3 per cent. sol.)	2.0	3.0	3.0	3.5
Pyrethrins (0.1 per cent. sol.)	—	—	0.5	1.0
Pyrethrins (2.0 per cent. sol.)	31.0	33.0	—	—

J. R. BURRINE

POTTER C. & GILLHAM E. M. Effects of Atmospheric Environment before and after Treatment, on the Toxicity to Insects of Contact Poisons. I. *Ann Applied Biol* 1946 May, 33 No 2 142-59 7 figs. [16 refs.]

The authors discuss the influence of temperature and humidity on precise laboratory testing of insecticides. Experiments are recorded in which the effects of keeping an insect cool or warm before and after spraying are related to the mortality caused by different contact insecticides in various media. The insect used throughout was the flour beetle *Tribolium castaneum* which was reared at 80°F (27°C).

It was found that exposure of the insects to cool conditions (50-60°F) or warm conditions (80°F) for one to twenty four hours before spraying did not have a great effect on the results. However insects kept under warm conditions after spraying were much more resistant to most of the insecticides tested than those kept under cool conditions. The actual ratios of potency of the different insecticides were as follows —

Poison	Medium	Ratio (potency of insecticide with cold storage after treatment as proportion of that under hot)
Pyrethrins	Aqueous	2.67 and 5.01 (2 expts.)
Pyrethrins plus Terpineol		7.21 and 6.90
Lauryl thiocyanate	Ethylene glycol Oil	1.43
Nicotine		1.23
Dinitro-o-cresol		1.46
DDT		2.61
Wakefield white oil ..		0.87

It will be observed that the only spray which caused greater mortality under warm conditions was the chemically inert Wakefield white oil.

It is believed that this effect of temperature must be referable to the physiological condition of the insect rather than to any direct physical action on the insecticide.

J. R. BURRINE

LARSEN Ellmör B & THOMSEN M. The Influence of Temperature on the Development of some Species of Diptera. Reprinted from *Idensk. Medd. fra Dansk naturh. Foren.* 1940 v 104 73 pp 18 figs. [39 refs.]

It is difficult to obtain accurate figures for the rate of development of flies which breed in dung and the optimum conditions cannot be precisely defined. Even when experiments are carried out in a thermostat fermentation may raise the temperature of the medium or evaporation may lower it and so invalidate the results. This paper is an account of very extensive experiments in which every attempt was made to eliminate these sources of error. Five species of diptera whose larvae live in dung were used: *Musca domestica*, *Stomoxys calcitrans*, *Lyperosia irritans*, *Harmatobia stimulans*, *Scatophaga stercoraria*.

With *Musca domestica* the minimum duration of the pre-imaginal period was 6.9 days at 33°C. Above this temperature there was some retardation and 40°C was too hot causing 100 per cent mortality. Development was slowed down by temperatures below 33°C to 15.66 days at 21°C and 64 days at 14.2°C. The developmental zero was in the region of 12°C, though some development occurred at as low a temperature as 9.2°C. The various stages of development—egg, feeding larva, pre-pupa, pupa—were affected in a roughly proportionate manner.

*Stomoxys calcitrans* developed most rapidly at 31.4°C. with a pre-imaginal period of 10.75 days. The rate for the whole zone of temperature from 29°C. to 33°C. was too hot causing 100 per cent mortality. Development was slowed down by temperatures below 33°C. to 15.66 days at 21°C and 64 days at 14.2°C. The developmental zero was about 12°C. Above 33°C. there was a marked retardation, and 35°C. proved fatal. At 15.7°C. development took 44 days. The developmental zero was about 12°C. There was no indication of a diapause occurring in either of the above species.

*Lyperosia irritans* was more difficult to rear in the laboratory. The shortest duration of the pre-imaginal period was 7.54 days at 32.3°C. A sudden drop in temperature below 18°C. seemed often to induce a pupal diapause.

*Harmatobia stimulans* is also difficult to rear in the laboratory. This species was adversely affected by much lower temperature than the others a fact probably correlated with its scarcity during the summer and its commonness in spring and autumn. The maximum rate of development (pre-imaginal period 11.1 days) occurred at 28.3°C. The threshold of development was at about 9°C. A diapause may possibly occur during development.

*Scatophaga stercoraria* was found to be even more easily harmed by high temperatures. The shortest pre-imaginal development, 15.38 days was found at 23.3°C. At 27°C. and above all were killed. The threshold of development was about 2°C.

Kenneth Mellanby

SWEETMAN H. L. DDT as a Spot Treatment for Flies. *J. Econom. Entom.* 1946 June v 39 No 3 330-81 [13 refs.]

The author observes that if one is treating buildings with DDT in order to reduce domestic flies it is sufficient to spray the particular places where flies settle or concentrate. He says that he has used ~25% DDT in white or odourless kerosene [which is not possible it is about five times more than a saturated solution].

P. A. Buxton

BRUCK, W. G. & BLAKEBLAKE, E. B. DDT to control Insect Pests affecting Livestock. *J. Econom. Entom.* 1946 June v 39 No. 3 367-74 1 fig.

- UNSWORTH K & GORDON R. M. The Maintenance of a Colony of *Phlebotomus papatasi* in Great Britain. *Ann Trop Med & Parasit* 1946 July v 40 No 2 219-27 3 figs. [24 refs.]

Several workers have maintained cultures of *Phlebotomus papatasi* in tropical and subtropical countries but there has been no strain maintained for long in this country notwithstanding the medical importance of the species. The classical methods essentially involved keeping the immature stages at the correct humidity and proper feeding of the adults on blood. By means of such technique five generations of *P. papatasi* have now been bred in Britain with a continually increasing population. However this method was so time-consuming that a more automatic technique has been devised. The breeding chamber in this case is inside a large block of porous cement which is soaked in water and thus ensures the correct humidity. Each day a baby rat strapped to a board is inserted to feed the adults. The larvae live in soil and in rabbit faeces at the bottom of the breeding chamber. This technique has been successful the culture being maintained with the minimum of supervision though it is as yet not possible always to ensure the production of very large numbers of flies.

Kenneth Mellanby

- KIRK R & LEWIS D. J. Taxonomy of the Ethiopter Sandflies (*Phlebotomus*). II. Keys for the Identification of the Ethiopter Species. *Ann Trop Med & Parasit* 1946 July v 40 No 2 117-29 56 figs.

The paper is without doubt valuable as a summary of the present state of knowledge. In all there are rather over forty known species from Africa south of the Sahara. The authors have excluded a number of other names on the ground of wrong identification or because they are synonyms.

The body of the paper consists of keys of adult males and females of the three subgenera, *Phlebotomus*, *Sintonius* and *Prophlebotomus*. It is assumed that one knows the subgeneric characters and can refer a specimen to one or another of these.

P. A. Buxton

- DAMASCENO R. G. CAUSEL O. R. & AROUCK, Regina. Estudos sobre Flebotomus no Vale Amazônico. Parte V. Descrição de *F. williamsi*, *F. deansii*, *F. carvalhoi*, *F. lopezi*, *F. castanheirai*, *F. farnazi*, *F. basilyi* e *F. campbelli* (Diptera Psychodidae). [Studies on *Phlebotomus* in the Amazon Valley. Part V.] *Mem. Inst. Oswaldo Cruz* 1945 Aug v 43 No 1 1-30 47 figs. (39 on 8 pls.) [14 refs.]

- D. ANDRETTA, M. A. V. & D. ANDRETTA C. Jr. As espécies neotropicas da familia Simuliidae Schiner 1864 (Diptera Nematocera). I.—*Simulium* (*Eusimulium*) *orbitale* Lutz 1910 *Simulium* (*Eusimulium*) *pinotoni* sp. n. e *Simulium nigricornum* Macquart, 1837 sp. inquirendae. [South American Species of the Simuliidae.] *Mem. Inst. Oswaldo Cruz* 1945 Aug v 43 No 1 85-152. Numerous figs. on 19 pls. & 2 maps. [18 refs.] English summary (7 lines)

- DENCKELL, R. A Study of an Insect Cuticle—the Larval Cuticle of *Sarcophaga falcata* Pand. (Diptera). *Proc. Roy. Soc. Ser. B.* 1946 Aug 7 v 133 No. 872, 348-73 7 figs. (3 on 1 pl.) [58 refs.]

- MALDONADO CAPRILES J. The Fleas of Puerto Rico. *Puerto Rico J. Pub. Health & Trop. Med.* 1945 Dec. v 21 No 2, 173-83 8 figs. [Refs. in footnotes.] [Spanish version 184-92.]

- SWEETMAN H. L. DDT to control Cat and Dog Fleas and Dog Lice. *J. Econom. Entom.* 1946 June v 39 No. 3 417-18

BUSHLAND R. C. Insecticides applied to Forest Litter to control New Guinea Chiggers. *J Econom Entom* 1946 June, v 39 No 3 344-7

Since DDT when sprayed from the air or otherwise, was successfully used to control mosquitoes over a wide area, many attempts have been made to control other vectors of diseases in a similar manner. The experiments carried out by the author in New Guinea were made against two species of trombiculid mite *Schönopastia pusilla* Womersley and *S. Mexicana* Gunther they cause "scrub itch" but have not been proved to carry the rickettsia of scrub typhus. It is believed, however that scrub typhus vectors would respond in a similar way.

An area in the New Guinea forest where mites abounded, so that up to about thirty could be collected from the boots in five minutes when a man crouched on the ground was treated partly with 40 U.S. gallons [40 U.S. gallons=32 Imperial gallons and partly with 80 U.S. gallons of 5 per cent DDT in diesel oil per acre and also partly with similar quantities of diesel oil alone. Other tests were made with 5 per cent diphenylamine and 5 per cent. diphenylene both at the rate of 80 gallons per acre. The ground was also dusted with 5 per cent DDT in calcium carbonate 320 pounds being applied to an acre.

The results of all these tests were similar. There was a temporary cessation of activity but living mites were always found within three days of spraying and within about a week normal activity had been restored. The diesel oil alone was quite as successful as any of the insecticides. [It should be noted that the rate of application of DDT was several hundred times as great as has been shown to be effective against mosquitoes and yet it had no noticeable effect on the mite population.]

Kenneth McIlanby

SNYDER, F. M. & MORRIS F. A. Materials as Effective as Benzyl Benzoate for Impregnating Clothing against Chiggers. *J Econom Entom* 1946 June v 39 No 3 385-7

Dimethyl phthalate dibutyl phthalate and benzyl benzoate, when used to impregnate garments have all been shown to be effective in preventing trombiculid mites from attaching to man. Dibutyl phthalate and benzyl benzoate have the advantage that they remain effective after the clothes have been washed [see this Bulletin 1946 v 43 922 923]. Extensive tests have been made at Orlando in Florida to find other substances equally or more effective and resistant to washing. Hundreds of substances have been tried, and discarded when either ineffective easily washed out or irritating to the skin. Uniforms were impregnated with the chemicals at the rate of 2 grammes per square foot (about 8 per cent of the weight of the cloth) and the wearers then sat or lay on the ground in an area abounding in mites (*Eutrombicula* spp). Volunteers wearing untreated uniforms showed several hundred mite attachments.

The following substances were at least as effective as benzyl benzoate — benzil phenyl benzoate benzoic acid 3 5-dimethyl phenyl ester 1 2 3 8 tetrahydro- $\alpha$ -methyl benzoic acid, 1 2, 5 6-tetrahydro- $\alpha$ -methylbenzyl ester phenanthrene  $\beta$ -methoxydiphenyl benzoic acid, alpha methylbenzyl ester benzoic acid phenyl-ethyl ester benzoic acid, 2-chlorophenyl ester

Kenneth McIlanby

WOMERSLEY H. A Revision of the Microtrombidinae (Acarina, Trombididae) of Australia and New Guinea. Reprinted from *Records of the South Australian Museum*. 1945 June 30 v 8, No. 2, 293-355 38 figs.

Previous work by WOMERSLEY and HEALING [see this Bulletin 1945 v 42, 324] has done much to elucidate the relationships of the Trombiculid mites

which cause scrub itch and which carry scrub typhus in the Austro-Malayan and Oriental regions. The present paper deals with the sub-family Microtrombididae. These mites are not themselves of medical importance but they are often confused with mites which are and their description will prevent much unnecessary field work by medical investigators. Eleven genera and forty species are described.

BERTRAM D S. An Apparatus for collecting Blood-Sucking Mites. *Ann Trop Med & Parasit* 1946 July v 40 No 2 209-14 2 figs

The mite *Liponyssus bacoti* has been successfully bred in the laboratory [see this *Bulletin* 1946 v 43 1080 and below]. One difficulty has been to isolate the mites from the sawdust and earth used as bedding for the cotton rats which are used to feed the mites. The apparatus here described consists of a sample tube to hold the infested sawdust etc. An electrically-heated coil moves slowly along the tube and this drives the mites before it into a collecting tube. The whole is mounted on a trolley and works automatically. The heated coil moves at a rate of rather less than half an inch a minute and so takes from one to two hours to traverse the three foot sample tube. The operator need only attend to the apparatus at the start and finish of the operation. Substantial numbers of mites may be collected in a typical case 113 mites, of which 60 were females were isolated. Practically all adults are evidently collected some nymphs are found but larvae (which are relatively inactive) are not. The eggs are presumably destroyed by the heat.

Kenneth Mellanby

BERTRAM D S. LANSWORTH K & GORDON R. M. The Biology and Maintenance of *Liponyssus bacoti* Hirst 1913, and an Investigation into its Role as a Vector of *Leishmanoides carinii* to Cotton Rats and White Rats, together with some Observations on the Infection in the White Rats. *Ann Trop Med & Parasit* 1946 July v 40 No 2 228-54 12 figs on 1 pl. [20 refs]

The blood-sucking mite *Liponyssus bacoti* has been shown to be a vector of filariae and also to be easily reared in the laboratory [see above]. This paper describes a similar technique for bearing the mites with full descriptions of the means used for handling individual specimens for transmission experiments.

The life-cycle of the mite is described in detail and illustrated with photographs. The life-cycle consists of the following stages: adults of both sexes, the egg which develops parthenogenetically in the absence of males, the six-legged larva, which moults without feeding, the protonymph, a blood-sucking stage, the non-feeding deutonymph. The whole cycle can be completed in ten days and the mites breed so rapidly that the infestation may kill the host.

Adult mites fed on rats infected with the microfilariae of *Leishmanoides carinii* often become themselves infected, though only a small proportion of the worms develop to later stages. Nymphs appear not to become infected.

The cotton rat has previously been shown to be easily infected by *Leishmanoides* transmitted by *Liponyssus*. The white rat may also be infected, and the microfilariae have been found in the pleural cavity and the heart blood, though not in the peripheral circulation seventy four days after exposure. However many of the worms in white rats as opposed to cotton rats which are easily infected were dead fragmented and encapsulated and a marked cellular reaction was observed in the host. It appears probable that the white rat may therefore be unsuitable for chemotherapeutic research.

Kenneth Mellanby

COOLEY R. A. *Note on the Tick, Ixodes angustus* Neumann. [Research Notes.]  
*J Parasitology* 1946 Apr v 32, No 2, 210.

This tick has been found to bite man. It has not been incriminated as a transmitter of human disease.

SMITH C. V. & GOUCK, H. K. *Observations on Tick Repellents.* *J Econom Entomol* 1948 June v 39 No. 3 374-8

The authors describe experiments in which men were exposed under natural conditions in places in the Southern United States in which ticks (generally *Imblyonoma*) were abundant. The clothes were treated with a considerable number of repellent and insecticidal substances. It was found that dimethyl phthalate, benzyl benzoate, and Indalone were generally fairly effective for a period of several weeks. Pyrethrum in kerosene was effective but for a much shorter period. DDT appeared to be without effect. Untreated controls were observed in each experiment. The dose of repellent is not stated.

The work was then extended to considerable field tests: the numbers of men in each not being stated. These experiments seem to show that against the same tick, Indalone and dimethyl phthalate are the most effective of the substances tested. A high degree of protection is obtained if one treats only the edges or apertures in garments but complete protection was seldom or never obtained. The repellents are more lasting if put on garments than on skin.

P. A. Buxton,

## LABORATORY PROCEDURES

BENDA, R. & FRANCHET, F. *Injectons intra-médullaires osseuses.* [Injections into the Bone Marrow.] *Semaines des Hôpitaux de Paris.* 1948 Sept 7 v 22, No 33 1571-7 8 figs. [45 refs.]

The authors list a number of substances for injection which may be given by introduction through the bone-marrow. They describe the methods employed and state that this route is equivalent to the intravenous route.

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

KAUNZIE W. H. *Social Medicine in the Tropics.* *Practitioner* 1948 Aug v 157 No 928 123-30

The points made by the Chief Medical Adviser to the Secretary of State for the Colonies, in this paper are as follows. The standards of living, diet and housing of the indigenous people of most of the Colonies are poor, especially in the urban areas. Even in rural agricultural areas the crops grown, which may be suitable to local climatic conditions, are quite often not nearly so suitable to human needs and malnutrition is frequently present in the people. Housing is usually bad, water supplies are contaminated and sanitation primitive. The people, therefore, though prolific are unhealthy and consequently apathetic, and there is high mortality.

The diseases from which these people suffer are either those spread throughout the community—for instance insect borne water borne or infectious diseases—and those which are not necessarily transmissible from one person to another. In the early days of the medical services in the Colonies emphasis was naturally laid on curative medicine and of this there was more than enough to occupy the whole time of the medical staffs but as the transmission of the great tropical diseases became more clearly understood the emphasis gradually shifted towards prevention. It is the author's argument that the attitude of the medical services should more and more lean in this direction.

Prevention has been attempted in different ways—by campaigns against individual diseases (which have often failed because they were not integrated or continued) or by intensive campaigns against all diseases. For the latter a team of workers concentrates on a limited area, introduces protected water supplies conservancy systems control of disease-carrying insects good housing efficient agriculture and gives such treatment as may be necessary. Success depends on the co-operation of the people themselves, and before this can be obtained they must be educated to understand and believe in the efforts made. When the intensive work has been completed the team moves elsewhere and the permanent staff undertakes the maintenance of the new conditions. Success in these schemes depends upon the local doctor the local nurses and their assistants who are most closely in touch with the people and who can stimulate and maintain interest in the general welfare but these doctors nurses and assistants need training in social medicine and in the appreciation of the influence of total environment on health.

[Readers will be reminded of several tendencies in the development of measures to improve the health of tropical peoples, which have become apparent in recent decades. Health units have been developed (not least by the author) in Central and South Africa Mauritius and Ceylon the great undertaking of the Anchau Settlement in Nigeria has proved its worth and the Foréarni service of the Belgian Congo has for long given a stimulating lead. It is surely on the lines here indicated that progress must be sought.] *Charles Wilcocks*

**MANSON BAHR, P.** *Tropical Medicine in the British Empire. Suggestions for the Future.* *Nature* 1946 June 29 858-60

In this paper in which Sir Philip Manson-Bahr points out that as a result of the war the number of patients returning to Britain with tropical diseases is very high, two constructive suggestions are made. The first is that as an aid to teaching there should be created a central institution at which strains of tropical parasites and their intermediate hosts should be maintained so that an abundant supply of teaching material could be available for the various schools at which tropical medicine is taught. This institution would be a miniature zoological garden with hot houses, animal houses stables and laboratories the site could be in some rural spot within reach of London. Snails, *Cyclops* mosquitoes and flies and many other animals could be bred and maintained under optimal conditions.

The second suggestion is that since there is in Britain a paucity of pathological specimens of tropical interest whereas the laboratories of the great tropical centres—Colombo Rangoon Singapore Shanghai and Hong Kong—possess ample materials an expedition should be sent to visit these and other places to arrange for proper collection and despatch of specimens to the British schools of tropical medicine.

[It would seem that these very practical suggestions should receive careful consideration if they were adopted, their value to teachers might well be enormous.] *Charles Wilcocks*



MAXSON-BAHR, P. The Post-Graduate Teaching of Clinical Tropical Medicine. Reprint of Chapter XVII pp. 361-73 from Albert Schweitzer Jubilee Book. 1946 London Jas. Clarke & Co. Ltd., Wardrobe Place, Carter Lane E.C.4

In this short contribution to the Albert Schweitzer Jubilee Book the author sets out some of his views on the influence of the recent war on medical teaching and on the steps which could be taken to improve the teaching of tropical medicine in Britain. He refers especially to the needs of students from abroad. His remarks on the collection of material in tropical countries are similar to those already recorded.

Charles Wilcocks.

BOYD W. S., STUBBS T. H. & WEINSTEIN P. P. The Tropical Disease Education Program of the United States Public Health Service. *Pub. Health Rep* Wash. 1946 May 17 v 61 No. 20 707-11

The most important diseases brought to the United States by men returning from tropical war service are thought to be malaria, amoebiasis filariasis, hookworm infection, leishmaniasis, schistosomiasis and hydatid disease. The American Society of Tropical Medicine has therefore requested the Surgeon General of the U.S. Public Health Service to consider —

(a) The organization of several teaching teams to visit State and other laboratories for the instruction of personnel in techniques of the laboratory diagnosis of the common tropical diseases.

(b) The dissemination of appropriate articles on the diagnosis and treatment of tropical diseases through its district directors to the practicing physician by means of State and local public health and medical publications.

(c) The formation of a library of teaching films on tropical diseases to be loaned to medical societies and other appropriate organizations.

As a result a Tropical Disease Education programme has been developed in Atlanta, and plans have been made to offer intensive training in the diagnosis of parasitic diseases to technicians already employed by State and local health department laboratories. The course lasts six weeks of which the first two are devoted entirely to the microscopical diagnosis of malaria, and the remainder to the study of other parasites as they are found in clinical human material. This course is to be repeated every three months so long as it is needed, and will be flexible to meet particular needs. An extension service has also been devised, by which stained specimens are sent from time to time to 105 laboratories in 43 States, so that the accuracy of the technicians may be checked. Specimens are also sent to teaching centres. The Diagnostic and Training Centre at Atlanta now also offers a consultative diagnostic service.

A second objective of this service is to further the instruction of medical men in the subject of tropical medicine, and for this purpose it has concentrated upon the development of visual materials—photographs lantern slides and films—to be used in teaching centres and at meetings of medical societies.

Charles Wilcocks

ANDREWS J. M. The United States Public Health Service Communicable Disease Centre. *Pub. Health Rep* Wash. 1946 Aug 16 v 61 No. 33 1203-10

This seems to be an account of the organization and programme of the Centre in Atlanta referred to in the preceding abstract though the names given to the centres are not the same. The Communicable Disease Centre has taken over the functions of the Office of Malaria Control in War Areas and deals largely with diseases common in the tropics and transmitted by insects the author

points out that very large numbers of Americans infected with these diseases are returning or have returned from military service in the tropics and that there is a constant danger of the introduction of infected persons or of non-indigenous vectors into parts of the United States in which the diseases could spread or the vectors multiply. Moreover when the need for medical men and others skilled in parasitology and tropical diseases was felt during the recent war the number available was small.

The development of the centre is summarized in three categories — (1) Training and training-aid production (2) Epidemiologic and laboratory services (3) Operational services. Training in the control of malaria, typhus plague etc. and in the diagnosis of these infectious is offered to State and local health officers. It includes the usual methods and the production of articles charts exhibits lantern slides and films. The epidemiological and laboratory services provide the means for instruction and for investigation of outbreaks of disease. mobile laboratories are available. One function will be the evaluation of techniques. The operational services will deal with the control of diseases and the testing of material and equipment including insecticides. These services will be available for emergency control and will also provide demonstrations of methods in appropriate areas.

The author notes that by 1945 upwards of half a million American soldiers had contracted malaria chiefly due to *P. vivax* and that these men diffused on return over the whole country could well establish the disease in new communities. The other possible infections in returning soldiers are also considered in relation to spread within the United States.

Most of the expenditure (70-80 per cent.) of the Malaria Control in War Areas organization has been accounted for by labour. Special investigations of operational significance were carried out in association with the National Institute of Health the Tennessee Valley Authority and other organizations. These wartime operations are rapidly diminishing but it is felt that a basic organization of physicians engineers and biologists should be retained partly to avoid repetition of the situation in 1942 when there were not enough competent teams to control malaria in overseas forces, partly to deal with infections introduced into the United States and partly to combat certain endemic diseases notably murine typhus sylvatic plague and insect borne virus infections which are progressively infiltrating and entrenching themselves in new sections of the United States.

Charles W. H. Wicks

RHODESIA SOUTHERN Report of the National Health Services Inquiry Commission 1945. pp iv + 124 1946 Salisbury Rhodesian Printing and Publishing Co. Ltd.

The Commission consisted of Professor C. F. M. Saint (Chairman) and four members the terms of reference covered enquiry into the following matters —

(i) The provision of an organised National Health Service in conformity with the modern conception of Health which will ensure adequate medical, dental nursing and hospital services for all sections of the people of Southern Rhodesia.

(ii) The administrative legislative and financial measures which would be necessary in order to provide Southern Rhodesia with such a National Health Service.

It would not be possible within a short space to give even the headings of this comprehensive report and those who are interested in the subject should consult the original. The Commission have made recommendations for the development of the medical services which, if carried into effect, would exercise a profound effect on the health of all sections of the people.

They have evidently been influenced by the schemes prepared in the Union of South Africa and by the Foréani service of the Belgian Congo. There is much evidence of the need to integrate the health services with those relating to agriculture and animal husbandry.

This report is one more sign of the need felt throughout Africa, for a revision of existing organizations in relation to health. There is little doubt that in the near future that continent as a whole will be much better served than hitherto.

Charles Wulcock.

MOTOUILLE L. Quelques statistiques médicales et démographiques concernant la main-d'œuvre indigène de l'Union Minière du Haut Katanga. (Some Medical and Demographic Statistics relating to the Native Craftsmen in the Upper Katanga Mines.) 1925-1944. *Ann Soc Belge de Méd Trop* 1946 June 30 v 28 Nos 112, 81-5.

MANSON J M S. The Maldives Islands and their Inhabitants. *J Roy Nav Med Serv* 1946 Apr v 32 No 2 105-12 6 figs [10 refs.]

There is little available information on health conditions in the Maldives Islands and the present communication is therefore of particular interest. The islands comprise a group of coral atolls and individual islands 400 miles south west of Ceylon. The people are of Arabian, Indian and Ceylonese origin, and are Moslems. The population of the southern islands numbers 14,500 and as a rule the people are mostly concentrated in one village on each island. The houses are primitive with roofs of iron thatch or tiles, the floors are of coral sand which is removed and replaced frequently. Beside each house is at least one well, for drinking water, but there is also usually a second, for washing. Clothing is simple: the ordinary people do not wear shoes or sandals which are the prerogative of royalty. There is no caste system, but social distinctions exist: the Sultan is the ruler and his Cabinet consists of men closely related to him.

Diet consists chiefly of rice which is all imported, and of the products of the rather poor soil—coconuts, papayas, bananas, bread-fruit, sweet potatoes, yams, pumpkins, limes and mangoes—(owls (with their eggs) and fish. Toddy is made from the young shoots of coconut trees, but is consumed fresh: no alcoholic liquor is allowed. Education is slight and the people do not approve of new ideas: it is forbidden to introduce modern inventions. Modern medical attention is not available. The commonest malady is chronic ulceration of the legs, but malaria, filariasis, elephantiasis and anaemia are prevalent. Amoebiasis, bacillary dysentery, tuberculosis, bronchitis, asthma, polyomyelitis and leprosy are also mentioned.

During the war scrub typhus became of great importance. It is endemic in the Maldives Islands and caused much trouble among the British forces, who were stationed there. The papers by HAY [this Bulletin 1945 v 42, 109] and ZAIR [ibid 111] refer to the Maldives: there were many cases of scrub typhus in men of the Royal Navy and though the case-mortality rate was not high, the morbidity rate was considerable. The larval mites concerned in transmission were probably *Trombicula deliensis*, but proof of this could not be obtained. In the indigenous people there is no evidence that scrub typhus is common, but infections are probably acquired in childhood.

The author discusses malaria, which is prevalent. [He states that the vector is *Anopheles fascioides*. No anopheline species of that name is known to the reviewer, nor is *fascioides* so far as can be ascertained, a synonym of any other species. COVELL (*J Malaria Inst. of India* 1944 v 5 424) notes that *Anopheles tessellatus* is the only anopheline so far recorded from the Maldives Islands, and that it is responsible for the transmission of malaria there: it breeds in shallow freshwater wells. No doubt *A. tessellatus* is the species meant.]

Charles Wulcock.

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Bl	Blackwater	Mal	Malaria
B.R.	Book Review	Misc. Dis.	Miscellaneous Diseases
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Def Dis	Deficiency Diseases including Epidemic Dropsy	Pl	Plague
Don.	Dengue	Prot	General Protozoology
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Dys	Dysentery (Bacillary and Unclashed)	R.F.	Relapsing Fever and other Spirochaetoses
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		Ya.	Yellow Fever

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 Belkin, J. N. (333) (Ent.)  
 — Knight K. L. & Rareboom L. E. 6 (Mal.)  
 Bell E. J. with Blake Marcy Seflusk & Kohls 327 (Typh.)  
 — with Mackie Davis Fuller Knapp Stehracker Stager Traub Jefferson Mills-paugh, Anstrian Kohls Wei Hel & Grahham 917 (Typh.)  
 — & Plotz, H. 434 (Typh.)  
 Bell, F. R. & Jones E. R., (1123) (Typh.)  
 Bell J. E., Jr & Boone, J. A., 377 (Vma.)  
 Beltrán E. (820) (Mal.)  
 — with Leon & Larcenas M., 1017 (Mal.)  
 Benda, R. & Franchet, F., 1193 (Lab.)  
 Bengtson, I. A. 20 651 (Typh.)  
 — Topping N. H. & Henderson R. G., 19 (Typh.)  
 — with — & — 20 21 (Typh.)  
 — with — & Shear 18 (Typh.)  
 Bennett, B. L., with Plotz & Reagan 920 (Typh.)  
 — with — & Wertman, 725 (Typh.)  
 Bennett, R. E. with Lawrence 36 (Dys.)  
 Bensimon, T. with Picard, 42 (Am.)  
 Bent M. J. Turner E. L. Holloway G. D. & Cuff J. R. 253 (Misc. Dis.)  
 Ber M. with Adler & Tchernomoretz 114 (Leish.)  
 Berberan D. A. 18 (Leish.) 653 (Am.) 939 (Hel.) 1105 (Mal.)  
 Bercovitz Z. T. 406 (Mal.)  
 Berg W. V. 242 (Haem.)  
 Berge C. with Le Chanton 915 (Typh.)  
 Berger E. & Brzezinski S. 549 (Typh.)  
 Berger L. Beadry M. & Gaumond E. 150 (Der.)  
 Bergeret, C. with Despujols Calmet & Rouvier (253) (Misc. Dis.)  
 Berkowitz S. 157 (Misc. Dis.)  
 Berlin, C. 856 (Der.)  
 Berman, R. L. with Friedheim 1124 (Typh.)  
 Bermudez, D. with Convit, Arulay & Salgado 457 (Lep.)  
 Bernard, L. with Cavallion Boyer & Delcourt, 544 (Typh.)  
 Berry J. F. with Zalametis & Ingraham 748 (R.F.)  
 Berry M. G., with Johnson 331 (Hel.)  
 Bertaux, M., with Vincke Parent & de Meulenaere 291 (Mal.)  
 Bertram, D. S. 1197 (Ent.)  
 — Unsworth K. & Gordon, R. M., 1197 (Ent.)  
 Bethes W. R. Jr with Brown & Stoffer 939 (Hel.)  
 Bowler G. 1136 (1 F.)  
 Bhatnagar S. S. & Shrivastava D. L. 840 (Pl.)  
 Bhattacharjya, B. P. & Gaha G. S. 1178 (Oph.)  
 Bhattacharya, K. P., with Rudra 787 (Misc. Dis.)  
 Biaggi, V. with Oliver Gonzalez & Rivera León, 347 (Hel.)  
 Bianchi, A. E. 63 (Der.)  
 Bianco A. A., with Smith Stormont & Evans (1157) (Hel.)  
 Blen W. N. 363 (Def. Dis.)  
 Blier O. G. (870) (Vma.)  
 — with Arantes & Hartmann (670) (Vma.)  
 Bierbaum, O. S. with Moore Welch & Wright, 477 (Haem.)  
 Biering, W. L. with Wooster & Dick, 372 (Haem.)  
 Biochevel, S., 507 (B.R.)  
 Biggam A. G., 783 (Misc. Dis.)  
 Billmer J. (336) (Hel.)  
 Bilhaga, J. J., with Hall 445 (Am.)



- Brooks A C with Ahuja 478 (Vma.)  
 Bruce W G & Blakeslee E B (1104) (Ent.)  
 Brückmann C & Wertheimer E. 206 (Bl.)  
 Brueck J W with Burns & Moss 486 (Der.)  
 Brueckmann G & Wertheimer E. 334 (Am.)  
 Bruestsch, W L. (13) (298) (Mal.)  
 Brug S L. 283 (Mal.) 321 (Typh.) 1041 (Am.)  
 — & Vos J J T. 382 (Prot.)  
 Brumpt E. 4 (907) (Mal.)  
 Brumpt I C & Mackuf A C. 835 (Typh.)  
 Bruu Mlo with Montel & Marhangeas Mlle 454 (Lep.)  
 Brunsing H A. with Gordon Marble Engstrom & Lippincott 1007 (Mal.)  
 Bruwer T with Palley 1083 (Reports etc.)  
 Brzezinska S with Berger 543 (Typh.)  
 Buchan R A. 231 (Hel.)  
 Buckland F E Dudgeon & Edward D G ff Henderson-Begg, A. MacCallum F O Niven J S F Rowlands I W & Van den Ende M with Bargmann, H E. Curtis E E & Shepherd M A. 438 (Typh.)  
 Buffa F & d Arcangelo D (1077) (Misc Dis.)  
 Bugher J C. 215 (A F.)  
 Bull Health Organisation (607) (Reports etc.)  
 Bull U.S. Army Med Dept 739 (Pl.) 925 (Den.)  
 Burch, G E. 593 (Heat Str.)  
 — & Winsor T. (676) (Heat Str.)  
 — with — 243 (Haem.)  
 Burgess R. W with Young Stubbs, Moore Ehrman Hardman & Ellis 5 (Mal.)  
 de Burgh P. 642 (Typh.)  
 de Burgh P M. 866 (Lab.)  
 Burke E. 317 (Leish.)  
 Burnham R C. 525 (Mal.)  
 Burns E. L. Moss E S & Brueck J W. 486 (Der.)  
 Burrell R. W with Deonier 410 (Mal.)  
 — with — Maple & Cochran 101 (Mal.)  
 — with Eide & Deonier 600 (Ent.)  
 — with Jones, Deonier & Knippling 530 (Mal.)  
 — with Wisecup & Deonier 530 (Mal.)  
 Burroughs A. M with Hawking (940) (Hel.)  
 Burrows R. B. (227) (Hel.)  
 Burt E. 827 828 1121 bis (Tryp.)  
 Bushland R. C. 922, 923 (Typh.) 1106 (Ent.)  
 Bussow H. 297 (Mal.)  
 Bustamante M E. Varela, G & Ortiz Mariotto C. 1134 (Typh.)  
 Bett E. M. & Hoffman A. M., 63 (Der.)  
 Butts D. C. A. 533 (Bl.)  
 Buxton P A. 305 (Mal.)  
 Byastrov P V. 294 (Mal.)
- Cadenat, J with Parrot & Mornet, (160) (902) (Ent.)  
 Cairo 753 (Hel.)  
 Calamet L. with Violle (730) (Typh.)  
 Caldeira, R. da G., 1183 (Lep.)
- Caldwell, J D. 1104 (Mal.)  
 Caldwell, M. H. with Spiess, Vilter & Koch 373 (Haem.)  
 California Mosquito Control Association 1079 (Ent.)  
 Callahan, W P., Jr. 234 (Prot.)  
 Calmet, L. with Despujols, Bergeret & Rouvier (253) (Misc. Dis.)  
 Calver K. M. with Browning Lockie & Walls, 633 (Tryp.)  
 Calvery H. O., with Fitzhugh Nelson & Glassman, 525 (Mal.)  
 Cambourne, F J C., with de Azevedo & Pinto (716) 828 (829) (Tryp.)  
 — & Simões J M. P., 95 306 (Mal.)  
 Cameron, G R., 835 (Typh.)  
 Cameron, T W M., 679 (Ent.) 1048 (Hel.)  
 Campana, Y with Desportes (746) (R.F.)  
 Campan, E. J with Hartman, Newcomb & Morrison, 718 (Tryp.)  
 Campbell D H & Cherkin A., 555 (Chi.)  
 Campos, J A., 834 (Leish.)  
 Campos, J S. & Souza P R., 47 (Lep.)  
 Canaan, T., 319 (Leish.) 340 (Lep.)  
 Cano C., with Loden, 731 (Typh.)  
 Cantrell, W with Coulston & Huff 205 (Mal.)  
 — with Kelsey Okidham & Gelling (625) (Mal.)  
 Carini, A., (1123) (Tryp.)  
 — & Springer L. (1170) (Der.)  
 Carpanelli J B., with Alecha & Ferreira, (196) (Am.)  
 Carrio C. C with Lippincott, Ellerbrook, Hesselbrock & Marble 1009 (Mal.)  
 Carrón, A. L. & Knott, J., 248 (Der.)  
 Carroll D G., 1047 (Hel.)  
 Caruthers L. B. 850 (Sp.)  
 Carter H. F., (1000) (Mal.)  
 — & d Aberra, V St. E., 683 (Ent.)  
 Carver R. K. with Wharton, 1079 (Ent.)  
 Casals J., 181 (Rab.)  
 Case R. A. M., 835 (Typh.) 1104 (Haem.)  
 Cassinelli, J F., with Lashier 567 (Hel.)  
 Castellanos L., with Woodruff (488) (Der.)  
 Carter W O with Mikkelsen & Koya, 1061 (Dof. Dis.)  
 Castillo, R. L., 262 (B R.)  
 Castle W B. with Watson 1067 (Haem.)  
 Castro A., with Antunes, 643 (Y F.)  
 de Castro Ferreira, L., with Laemmert, 33 (Y F.)  
 de Castro Palomino, J & Alfonso y Armenteros, J., 563 (Lep.)  
 Catana, A. 780 (Der.)  
 — & Kervran, P., 247 (Der.)  
 Cateno C. F., with Ellerbrook, Lippincott, Gordon & Marble, 628 (Mal.)  
 Cattani, R., Corcos, A. & Cohen, H., 337 (R.F.)  
 Caubet, P., 312 (Tryp.)  
 — with Roubaud 418 (Tryp.)  
 — with Stefanopoulos & Durodon, Mills., 417 420 (Tryp.)  
 Causey O R., with Damascano & Aroock, (1165) (Ent.)  
 — Deane L. V. & Deane, M. P., (189) (Mal.)  
 — & Mello, G B., 287 (Mal.)



- Cavaillon, A. Bernard, L., Boyer & Delacourt, 544 (Typh)  
 Cawron, F. G. (1190) (Misc. Des)  
 Ceraaldi, J. 190 (Rab)  
 Celsus, E. B. with Ruffin, Zarrow, Heider, von & Whitehead 188 (Rab)  
 Cerbasi, E. A. Pecoraro, V. & Rodolfo, A. 847 (Lep)  
 Cernigoi, G. & C. with Lima 47 238 (Lep)  
 Cerni, B. 749 (Lep)  
 Cerruti, H. 1129 (Lent)  
 Chamberl, M. & Mhappé 1122 (Plat)  
 Chikara, H. with Das Gupta & Lowe 34 (Plat)  
 Chikaravati, A. C. 833 (Lent)  
 Chitra, arya, V. H. with Sen Gupta, 833 84 (Lent)  
 Chitren, W. C. & Bal, r. A. B. (594) (Misc. Des)  
 Chafie, H. D. 835, 911 (Typh)  
 Chambers, G. with Schmitt & Alpina, 482 (Der)  
 Chandler, A. C. 1085 (B. R.)  
 Chandr, P. J. 658 (Lep)  
 Chapin, S. E. 844 (Am)  
 Charbonne, M. with Paul, 1159 (Hel)  
 Chartier, A. D. 224 (R.F.) (474) (Def. Dis)  
 351 (Typh)  
 — with Mason, Fisher 1106 (Misc. Des)  
 Chatterjee, J. B. with Das Gupta & Gangah 1093 (Harm)  
 Chatterjee, B. C. with Gupta, Paul & Ghose 130 (Chl)  
 Chatterjee, H. N. 555 (Chl) 722 (Lent)  
 Chatterjee, M. with Gupta & Pajya, 1138 (P)  
 Chaudhri, J. R. with Jacob 129 648 (Chl)  
 Chaudhri, R. V. & Bai Chaudhri, M. V. 843 (844) (Am)  
 Cheever, F. S. 649 (Dys)  
 Chelavencu, M. with Croca & Balul, 29\* (Mal)  
 — with — & Cristescu, 290 (Mal)  
 Chen, G. & Ceding, E. M. H. 318 (Tryp)  
 Chen, K. T., Tang, I. L. & Wang, M. C. (97) (Mal)  
 Chen, S. M. with Pang, Zuo & Peng, 326 (Typh)  
 Cheney, L., with Yoo & Greene, 521 (Mal)  
 Cherkin, A. with Campbell, 553 (Chl)  
 Chermock, R. L. & Muller, H. E. 808 (Lab)  
 Cherry, C. B. & Bartlett, A. G. 778 (Der)  
 Chesterman, C. C., 835 (Typh)  
 Chi, Ho, (1060) (Mal)  
 Chiao, S. M. 899 (R.F.)  
 Chippaux, C. & Chippaux Mathis, J. 788 (Prot)  
 Chippaux Mathis, J. with Chippaux, 783 (Prot)  
 Chopra, I. C., with Badhwar & Nayar 672 (Der)  
 — with Chopra, 304 (Mal)  
 Chopra, R. V. & Chopra, I. C. 304 (Mal)  
 Chorne, V. 341, 459 584 (Lep)  
 Chorley, J. K., 412 (Tryp)  
 Christophers, R., 684 (Reports, etc)  
 Chabkova, A. I., with Ananian, Anson & Kochanov, 13 (Mal)
- Chung, H. L., 321 (Typh)  
 Churchill, M. H. 473 (Def. Dis) 558 (Oph)  
 Chwatt, L. J., 5 (Mal)  
 Ciaravino, E., with Soda, 37 (Am)  
 Cifuentes, O., with Macchiavello, 23 (Typh)  
 — with — & Ovalle 1032, 1033 (Typh)  
 Cistrie, W. with Morae, Stabbe, Crowdr, Mackinnon, Blacklock, Engledow & Henderson, 70 (Reports, etc)  
 Cima, M. Balul, L. & Chelavencu, M. 292 (Mal)  
 — — — & Cristescu, A. 290 (Mal)  
 — with Ionesco-Mihalesti, 321 (Typh)  
 — & Meurobeanu, L. (210) (Typh)  
 — — — Badenski, A. Franke, M. & Monteanu, G. (210) (Typh)  
 — — — Monteanu, G. & Paraschescu, N. (10) (Typh)  
 Clancy, C. F. & Wolfe, D. M. 841 (Typh)  
 — with — Vanderhoeft & Cox, 735 (Typh)  
 Clapham, P. A. (233) (Hel)  
 Clapp, J. V. with Fay & Simmons 790 (Ent.)  
 Clark, E. M. with Craigie Watson & Maccomson, 914 (Typh)  
 Clark, J. H. with English, Shepherd, Marston, Knapcho & Robbin, (905) (Mal)  
 Clark, R. H. P. 1132 (Typh)  
 — & Dettia, D. H. 559 (Am)  
 Carlo, C. A. & Seiddon, I. B., 944, 1039 (Def. Dis)  
 Clarke, J. D. 1024 (Tryp)  
 Clara, G. 118 (Typh)  
 Clavero, G. & Gallardo, F. P. (117) (Typh)  
 Cleland, J. B. (42) (Am)  
 Clemo, G. R. Cocker, W. & Hornaby 5 (1054) (Hel)  
 Cline, J. F. with Spees, Vaher & Frommeyer 772 (Harm)  
 Clever, E. H. Joki, E. & Ronch, P. R. (1084) (Reports etc)  
 Clever, P. W. P. 1111 (Mal)  
 Coates, W. A. with Heidelberger & Mayer 1019 (Mal)  
 Coatsney, G. R. Cooper, V. C. & Trembley, H. L. 829 (Mal)  
 Coblenz, A., with Browning, Raphael & Klem, 848 (Typh)  
 Cochran, J. H. with Deemer, Burrell & Mapie 191 (Mal)  
 Cockrane, R. G. 1146 (Lep)  
 Cockburn, C. (586) (Hel)  
 Cocker, W. with Clemo & Hornaby (1054) (Hel)  
 Coda, D. (904) (Mal)  
 Codolencu, E. 1130 1131 (Typh)  
 — with d. Ignazio, 732, 1130 1131 (Typh) 1042 (R.F.)  
 Codomas, A. (539) (Lent)  
 Coelho, J. T. 1147 (Lep)  
 — with Vento 1180 (Lep)  
 Coggeshall, L. T. 295 (Mal) 832 (Hel)  
 — with Spector & Haviland 823 (Mal)  
 Cogswell, R. C. with Spees, Perry & Frommeyer 80 (Def. Dis)  
 Cohen, H. H. 784 (Hel)  
 Cohen, H. with Cattin & Corton, 337 (R.F.)  
 Cohen, J. with Rugiero, 326 (Typh)

- Cohen S. C. Emert, J. T. & Goss C. C. 595 (Misc. Dis.)  
 Coito A. de M. F. with de Meira & Girão 760 (Hel.)  
 Colas-Belcour J. with Ronbaud 383 (Ent.)  
 Colchester T. R. (591) (Reports etc.)  
 Cola, G. 566 (Hel.)  
 Cole H. N. with Luckiesh, Taylor & Sollmann, 675 (Heat Str.)  
 Cole L. C. 331 (Pl.)  
 Collier H. O. J. & Louni E. M. 1126 (Leish.)  
 Collignon, E. 307 (Mal.)  
 Collins D. L. with Glasgow 824 (Typh.) 962 (Ent.)  
 Collins R. h. 999 (Mal.)  
 Colonial Office 85 883 (B. R.)  
 Combescot de Marsaguet, G. with Le Gac & Sente 621 (Mal.)  
 Conejos M. with Arguello Pitt, 458 649 (Lep.)  
 Conge M. with Witt & Kauffmann, 749 (R.F.)  
 Connecticut State Department of Health 867 (Reports etc.)  
 Connell W. K. 164 (Reports etc.)  
 Convit, J. Azulay R. D. Bermudez, D. & Salgado P. 457 (Lep.)  
 Cook, C. D. & Hoffbauer F. W. 819 (Mal.)  
 Cook Islands, 75 (Reports etc.)  
 Cook, R. P. with Brodie Drysdale & McIntosh, 841 (Dys.)  
 Cooke W. T. Elkes J. T. Frazer A. C. Parkes J. & Peener A. L. P. 946 (Sp.)  
 Cooley R. A. 1193 (Ent.)  
 — & Rohls C. M. 864 (Ent.)  
 Coombes A. E. R. with Rogan S. 4 (Mal.)  
 Cooper G. R. Rein, C. R. & Beard, J. W. 1027 (Leish.)  
 Cooper W. C. with Coatsnev & Tremblev 629 (Mal.)  
 Cooperman J. M., Elvehjem, C. A. McCall K. B. & Ruegamer W. R., 772 (Haem.)  
 — Ruegamer W. R. & Elvehjem, C. A. (1067) (Haem.)  
 Corbett, A. J. with Settle & Pinkerton 27 (Typh.)  
 Corbyu, E. N. 76 (Reports, etc.)  
 Corcos, A., with Cattain & Cohen, 337 (R.F.)  
 — with Laigret, 739 (Den.)  
 Corma F. E. & Alsever W. D. 1167 (Der.)  
 Cornatzer W. L. with Hyker & McEwen 706 (Mal.)  
 Cornell, L., Pourvines I. & Moustardier G. 216 (Pl.)  
 Corradetti, A. (817) (Mal.)  
 Correa, R. R., (904 905) (Mal.)  
 Cottam, C. & Higgins E. 1014 (Mal.)  
 Cottor E., 72 (Reports, etc.)  
 Cottot, J. with Deschamps (766) (Hel.)  
 Cottrell J. D. & Hayward, G. W., 653 (Am.)  
 — & Peddie, J. J. G., 333 (Am.)  
 Coulston F., Cantrell, W. & Huff C. G. 205 (Mal.)  
 — with Huff, 1115 (Mal.)  
 Coupland R. 1090 (B.R.)  
 Courts, W. E. 136 (Am.)  
 Cowen, D. & Wolf, A., 678 (Prot.)  
 Cox, C. D. & Arbogast, J. L., 1187 (Misc Dis.)  
 Cox, H. R. with Irons, Topping & Shepard 924 (Typh.)  
 — with Wolfe Vanderscheer & Clancy 735 (Typh.)  
 Coxon, R. V. & Hayes, W., 406 (Mal.)  
 Craig, C. F. & Faust, E. C., 506 (B. R.)  
 Craig, B. with Heidelberg Mayer Alving, Jones Pullman & Whorton, 1013 (Mal.)  
 Craige J., 834 (Typh.)  
 — Watson D. W., Clark, E. M. & Malcomson M. E. 914 (Typh.)  
 Crauford Benson H. J., 633 (Typh.)  
 — & Macleod J., 638 (Typh.)  
 Cristescu A. with Cuca, Baliff & Chelarescu 290 (Mal.)  
 Cropper C. F. J. 38, 1141 (Am.) 232 (Misc. Dis.)  
 Croxatto H. (1069) (Vms.)  
 Crowdy R. E. with Moyne Stubbbs Citrine Mackinnon, Blacklock, Engledow & Henderson, 70 (Reports etc.)  
 Cruckshank, E. K. 1159 (Def. Dis.)  
 Cruz, E. with Pascale, 546 (Typh.)  
 Cruz, J. N. with Fernando & Ayrao 1181 (Oph.)  
 Cruz, W. O. & de Mello R. P. 680 (Hel.)  
 da Cruz Ferreira, F. S. (796) (Ent.)  
 — & de Mera, M. T. V., 863 (Ent.)  
 Cuff J. R., with Bent, Turner & Holloway 253 (Misc. Dis.)  
 Culbertson, J. T. with Rose & Lipman, 232 (Hel.)  
 — — & Oliver-Gonzalez J., 54 334 763 (Hel.)  
 Cullinan, E. R., 330 (Den.) 783 (Misc. Dis.) 944 (Def. Dis.)  
 — hekwick, A., Watts A. S. & Titman W. L. 942 (Def. Dis.)  
 da Cunha, A. M., 113 209 (Leish.)  
 — & Guimarães F. N., 562 (Ia.)  
 Curd F. H. S. with Basford & Rose, (1110) (Mal.)  
 — Davey D. G. & Rose F. L. 394 400 (Mal.)  
 — Davis, M. I., Owen, E. C. Rose F. L. & Tuoy G. A. P. (1110) (Mal.)  
 — & Rose F. L., (822 bis) (1110) (Mal.)  
 Curran, G. with Atchley Bacon & Davd, 160 (Lab.)  
 Currens, J. H. & Woodard R. C. (339) (R.F.)  
 Curtis, A. C. & Owens B. B. 486 (Der.)  
 Curtis E. E. with Bockland Dudgeon Edward, Henderson Begg, MacCallum, Niven, Rowlands vanden Ende Bargmann & Shepherd, 436 (Typh.)  
 Cutting, C. C. with Hanzlik, 820 (Mal.)  
 Cutting J. T. with Wright & Reppert, 781 (Heat Str.)  
 Czaczka, J. W., with Olitzki, Oleinik & Kutrenok, (635) (Typh.)

## D

- Daggy R. H. 1107 (Mal.)  
 Dahms, R. G. with Olson, (788) (Ent.)  
 Daley R., with Smart, 1160 (Sp.)  
 Damasceno R. G. Causey O. R. & Aruck, R. (1185) (Ent.)

- Davis I F 122 (Typh)  
 Dammun C J with F Jones, 1049 (Hel)  
 — with Weller 347 1185 (Hel)  
 Dammun B R with Johnson 915 (Typh)  
 Dargdale J H & Fitzgerald P J 576 (Hel)  
 Dant L J with Robertson Farmer  
 Norris & Heuser (1066) (Haem)  
 Dant W B with W von Paddock &  
 Gordon 1177 (H)  
 Dancy Browning C C R & W M 588  
 (Opb)  
 Darby W J 55 (H)  
 — & Jones L 41 (H)  
 — & Johnson H C 667 770 (Op)  
 Darnes J J 1182 (Opb)  
 Dase (Opb) B W L with J A (Chikara arts,  
 H 268 (Mal)  
 — a von R 1 (H)  
 — & H 1 (H)  
 Das (Opb) C K (Gangula b & Chatterjee,  
 J B 1004 (Haem)  
 Dasgupta S K (J N) (Lamb)  
 Datta with Bose (Chosh & Mitra, 1025  
 (Lamb)  
 Day A 581 (Misc. Dis)  
 Day D C 12 1010 (Mal)  
 — with Curd & Rose 304 400 (Mal)  
 Day T F 1151 (Lep)  
 Day T H with Adams, Macgregor & King,  
 Townsend & Ha and 407 (Mal)  
 — with Macgregor Adams, King Town-  
 send & Ha and, 402 (Mal)  
 Day J J (806) (Reports, etc)  
 Day J H with Atchley Bacon & Curran,  
 189 (Lab)  
 — with W A L 679 800 1182 (Ent)  
 Day B J 124 (Typh)  
 — J A (806) (Hel)  
 — D E & Pollard, M 1033 (Typh)  
 — D H S 1038 (H)  
 — with de Meillon, 866 (Ent)  
 Day D J & Sullivan T de S 1026 (Tryp)  
 Davis G E with Mackie Fuller Knapp,  
 Stensacker Stager, Traub, Johnson, Mil-  
 laner, Anstman, Bell, Kohls, Wei Ha &  
 Curran, 917 (Typh)  
 Davis H V & Neil, F C 779 (Der)  
 Davis J E (857) (Haem)  
 Davis M I (822) (Mal)  
 — with Curd Owen, Rose & Tney (1110)  
 (Mal)  
 Davis O T Harrell, G T & King, E. S.  
 (143) (Hel)  
 Davis W A 477 (Typh)  
 Dawson, A R 455 (Lep)  
 Dawson, J with Marston, 12 (Mal)  
 Dav C L Wood, E A & Lane, W F  
 (853) (H)  
 Deane L M with Cansev & Deane, (189)  
 (Mal)  
 Deane M P with — & — (199) (Mal)  
 Dearborn, E. H. & Marshall, E. H. Jr., 404  
 (Mal)  
 Debray J R, with Hillebrand, Larry &  
 Duguet, 858 (Hel)  
 Degaron, D W., (62) (Haem)  
 Depotte, J., 340 (Lep)  
 Del Pozo, E. C., González Q J & Méndez,  
 T H., (146) (Vms)  
 Del Valle Alemán S., with Sotolonga &  
 Alkono (50) (Hel)  
 Delcourt, with Cavallion, Bernard & Boyer  
 544 (Typh)  
 Delmanto, A (602) (Ent)  
 Delny L P (1080) (Ent)  
 Dehalla J 95 (Mal)  
 Demarest, C R with Heidelberg & Mayer  
 618 (Mal)  
 Denby E 145 (Haem)  
 Deneill R (1195) (Ent)  
 Dennison W & Evans, W (850) (Misc. Dis)  
 Denner C C & Burrell, R. W 410 (Mal)  
 — Maple, J D & Cochran, J H.,  
 101 (Mal)  
 — with Rud & Burrell, 600 (Ent)  
 — & Jones, H A 531 (Mal)  
 — with — Burrell & Knipping, 530  
 (Mal)  
 — with — Lundquist & Human, (625)  
 (Mal)  
 — Maple, J D Jones H A Hinchey E.  
 & Esda, P M 101 (Mal)  
 — with Wiscup 101 (Mal)  
 — with — Brothers & Esda, 1078 (Ent)  
 — with — & Burrell, 530 (Mal)  
 Derrick, E H with Morrison 31 (Typh)  
 — with Saxton & Hatcher 1160 (Der)  
 Deschamps, R (352) (Hel)  
 — & Cottet J (768) (Hel)  
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 — & Ferreira, L B (831) (Tryp)  
 — & de Freitas, L. Jr 108 (Tryp)  
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 vobole V. P. & Emerson, H. Jr. with Braun E., 624 (Mal)  
 vocation, A. with Sergeant & Parrot, (603) (Ent.)  
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 vonovick, R. Farrell, M. & Smith, F. 635 (Typh.)  
 — with Groupé, 635 728 (Typh.)  
 vorin R. P. 1057 (Hel.)  
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 — & Pittendrigh, C. S. 1001 (Mal)  
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Gupta, S. K. Chatterjee, B. C. Paul B. M.  
& Ghose R. N., 130 (Chl.)  
Gutiérrez Sánchez, E., 1110 (Mal.)  
Gwinner G. with Spies, Frommeyer Garcia  
Lopez & Lopez Toca, 949 (Sp.)

## H.

Haas V. H. Wilcox A. & Ewing F. M. 1114  
(Mal.)  
Habel, K., 192 (Rab.)  
Habibe M., 1129 (Typh.)  
Hackett, C. J., 835 (Typh.)  
Haddad N. 379 (Misc. Dis.)  
Haddow A. J. 79 80 (Reports etc.) 255  
863 (Ent.)  
Haig D. A., with Polson & Joubert, (854)  
(Vms.)  
Hailey H., 954 (Der.)  
Haurston, N. G. with Bang Ferguson &  
Graham, 350 (Hel.)  
— with Trager & Bang 821 (Mal.)  
Halawani A. & El Hordy, M. I. (1143) (Am.)  
— with Khalil Bey & Gamal Nor El Deen,  
50 (Hel.)  
— & Nor-el-Din G. 1109 (Mal.) (1143)  
(Is.) (1158) (Hel.)  
— & Iwna, A. 1142 (Am.)  
Halawany A. & Jabb, M. 540 (Leish.)  
Hall B. & Billings, J. J. 443 (Am.)  
Hamilton H. L. 320 434 734 (Typh.)  
Hamilton, T. S. with Johnson & Mitchell,  
691 (Heat Str.)  
— with Shields, Johnson & Mitchell, 691  
(Heat Str.)  
— with Spector (378) (Heat Str.)  
— with — & Mitchell, (378) 591 bis  
(Heat Str.)  
Hamilton Paterson J. L. with Piney 870  
(B.R.)  
Hammann, W. McD. with Florio Laurent &  
Stewart, 737 (Den.)  
Hampton, B. C. 554 bis (Pl.)  
Hamrah N. A., 631 (Am.)  
Hanzlik, P. J. & Cutting, C. C., 820 (Mal.)  
Hardcastle A. B., with Wharton, 1080 (Ent.)  
Harting, R. D. 105 (Tryp.)  
Hartman, V. F., with Young Stubbs  
Moore Ehlman, Ellis & Burgess, 5 (Mal.)  
Hartman, V. H. with Moore Young &  
Stubbs, 1002 (Mal.)  
Hargreaves W. H., 844 1040 (Am.)  
— with van den Ende, Lockett, Niven &  
Lounhoff, 918 (Typh.)  
Harley R. D. 1148 (Lep.)  
Harper F. 510 (B.R.)  
Harper J. O. with Garnham & Highton 736  
(Y.F.)  
Harrall, G. T. with Avera, Low & Fowler  
783 (Hel.)  
— with Davis & King, (143) (Hel.)  
— with Dingledine & Willis 837 (Typh.)  
— & Horro S. F. 635 (Lep.)  
— Wolff, W. A. Vennig W. L. &  
Reinhart, J. B. 923 (Typh.)

Harris J. R. & Hickey M. D., 138 (Hel.)  
Harris J. S. & Summers W. A., 569 (Hel.)  
Harrison C. V. with Fulton, 1123 (Tryp.)  
Harrison, D. C. with Gibson, 773 (Haem.)  
Harrison, G. F. 945 (Def. Dia.)  
Harvey A. M. Kuffler S. W. & Trodway  
J. B. 490 (Misc. Dis.)  
Haskins, W. T. with Lawton, Brady & Vasa,  
55 (Hel.)  
Hasseltine H. E., (453) 457 (Lep.)  
Hatcher F. with Saxton & Derrick, 1169  
(Der.)  
Hatoft, A. 632 (Ent.)  
Hanner C. R., with Brawley Walker Yost &  
Shivers, (405) (Mal.)  
Havard, R. E. with Adams, Macgrath,  
King Townsend & Davey 402 (Mal.)  
— with Macgrath, Adams King &  
Millet, 238 (Sp.)  
— with — — — Townsend &  
Davey 402 (Mal.)  
Haveaux, G. 1019 (Tryp.)  
Haviland J. W. with Spector & Coggeshall,  
823 (Mal.)  
Hawe P. 134 1140 (Am.)  
Hawking F. 380 (Misc. Dis.) 410 (Mal.)  
— & Burroughs, A. M., (940) (Hel.)  
Hay S., 364 (Lab.)  
Hayes, W. with Cowan, 406 (Mal.)  
Hayman J. M., Jr. with Behm, 762 (Hel.)  
— with Most, 1004 1005 (Mal.)  
— with — — — London, Kane Lavietes &  
Schroeder 1011 (Mal.)  
Haynes H. L., with Granett, 631 (Ent.)  
Hayward, G. W. with Cottrell, 633 (Am.)  
Hazelton, A. R., 1181 (Oph.)  
Headley A. E., with Boland & Hench, 597  
(Misc. Dis.)  
Heath, P. & Zoelzer W. W., 67 (Prot.)  
Heaton, C. E., (839) (Y.F.)  
Hegsted, D. M., with Williamson, McKibbin  
& Stare, 1009 (Mal.)  
Hendelberger M., Mayer M., Alving, A. S.,  
Crane, B., Jr., Jones R., Jr., Pullman  
T. N. & Whorton, M., 1013 (Mal.)  
— Contee W. A. & Mayer M. M., 1013  
(Mal.)  
— Mayer, M. M. & Demarest C. R., 816  
(Mal.)  
— Frost, C. Hinkle, J. A. & Rose, A. S.,  
1013 (Mal.)  
Heng, R., 520 (Mal.) 1074 (Misc. Dis.)  
Helleman, L., with Bovernick & Lindsay  
824 825 (Mal.)  
Heller F. F., 835 (Typh.)  
Hemmings, R. J., (1015) (Mal.)  
Hemphill, E. C. with Schuhardt, 748  
(R.F.)  
Hench, P. S. with Boland & Headley 597  
(Misc. Dis.)  
Henderson, D. G., with Rifkin, Colada,  
Zarrow & Whitehead, 183 (Rab.)  
Henderson H. D., with Moyne Stubbs  
Crowdy Citrine, Mackinnon, Blacklock &  
Engelwood 70 (Reports, etc.)  
Henderson, H. J. 457 (Lep.)  
Henderson, J. M. (205) 287 (Mal.)  
Henderson R. G., with Bengtson & Topping,  
19 (Typh.)



- Henderson, R. G. & Topping, N. H. 20 (Typh)  
 — with — & Bengtson, 20 21 (Typh)  
 Henderson Bagg, A. with Hockland, Dudrean, Edward, MacCallum, Arven, Rowlands & van den Ende, Bargmann, Curtis & Shepherd, 436 (Typh)  
 Hennard C. with van Hoot, Lewillon, Peel & Rodjostrensky 536 (Tryp)  
 — with Wansou, 23\* (Hel)  
 — with — & Peel, 253 (Hel)  
 Herbeval, R. with Drouot, Thomas & Tarré, 467 (Hel)  
 Herbst, P. A. & Kinney F. R. 959 (Misc Dis)  
 Hermans, F. H. 799 (Reports, etc)  
 Hermitte, L. C. D. 970 (Reports etc)  
 Hernández Morales, T. (228) 462, (1159) (Hel) 239 (Sp)  
 — & Diaz Rivera, R. 230 (Hel)  
 — & Oliver González, J. 1158 (Hel)  
 — & Pratt, C. H. 1043 (Hel)  
 — & Ruiz Costero, G. (228) (Hel)  
 — with Suárez 349 (Hel)  
 — with — & Diaz Rivera 496 (Lab)  
 Herish, J. (1190) (Misc Dis)  
 Hess A. D. with Metcalf, Smith, Jeffery & Ludwig, 102 (Mal)  
 Hesselbrock, W. B. with Lippincott, Ellerbrook, Carmo & Marble 1009 (Mal)  
 — with — Gordon, Gottlieb & Marble 523 (Mal)  
 Heuser, G. F. with Robertson, Daniel, Farmer & Norris, (1066) (Haem)  
 Hickey M. D. with Harris 135 (Hel)  
 Hicks, J. D. 1134 (Typh)  
 Higgins, L., with Cottam, 1014 (Mal)  
 Highton, R. B. with Garnham & Harper 736 (A F)  
 Hill, A. R. 833 (Typh)  
 Hill R. B. & Hill C. M. 1191 (Ent)  
 Hillebrand, P. Varay A. Delray J. R. & Dugout, Mme 656 (Hel)  
 Hilmy, I. S., 51 (Hel)  
 Hinchey E. with Decker, Maple, Jones & Lude, 101 (Mal)  
 Hindle J. A. with Headlberger, Probst & Rose, 1013 (Mal)  
 Hinds E. G. with Yule & Gold, 531 (Bl)  
 Hitti J. K. & Khanallah, A. A. 1137 (Dem)  
 Hoare, C. A. 317 (Leish)  
 Hobbs, H. E. & Forbes, F. A. 1179 (Oph)  
 Hocking, K. S. 681 (Ent)  
 — with Melville, Wilson & Glasgow 62 (Mal)  
 Ho-Duc Di, with Meyer, May & Dinh-Tung, Tong-That Tung & Dinh Van-Thang, 67 (B R)  
 Hodes P. J. & Wood, F. C. 66 (Misc Dis)  
 Hodge E. H. 43 (Hel) 684 (Reports, etc)  
 Hodgson, J. A. with Granot & Schaafsma, 676 (Vms)  
 Hoch, D., 256 (Ent)  
 Hoffbe, F. W. with Cook, 819 (Mal)  
 — with Fredenla, 97 (Mal)  
 Hoffman, A. M., with Britt, 63 (Der)  
 Hoffman, W. A. with Kralowicz & Artmayer 227 (Hel)  
 Hoffender A. J. with Parker 186 (Rab)  
 Hollins, C. 1133 (Typh)  
 Hollow K. with Finlayson, 378 (Vms)  
 Holloway G. D. with Bent, Turner & Cuff 253 (Misc Dis)  
 Holmes, E. G. 146 (Haem)  
 Hong, P. & Verdoorn F., 884 (B R)  
 van Hoot, L., (969) (Reports etc)  
 — Lewillon, R. Hennard C. Peel, E. & Rodjostrensky B. 636 (Tryp)  
 Horack, H. M., with Simmons, Wayne, Anderson & collaborators, 66 (B R)  
 Horcker B. L., 1085 (Haem)  
 Horgan E. S. & Sattu, M. H., 17 (Leish)  
 Horne, S. F. with Harrell, 655 (Lep)  
 Hornbrook, J. W. 741 (M)  
 Horns, R. with Adams & Eklund, 862 (Prot)  
 Horsey S. with Clemo & Cocker (1034) (Hel)  
 Horvath S. M. with Shelley 675 (Heat Str)  
 Hoskins, W. M. with Macy 601 (Ent)  
 Howe, C. D. & Duff, F. L. 523 (Mal)  
 Howell, K. M. with Knoll, 444 (Am)  
 Howell, W. L. 327 (Typh)  
 Howells, G. (334) (Am)  
 Howser J. W. with Vaughn & Shropshire (157) (Misc Dis)  
 Hoyson, H. M. with Boncovich & Walston, 763 (Lab)  
 Hubbard C. S. 498 (Reports, etc.)  
 Hudson, E. H. 931 (Ya)  
 Huff C. G. & Coniston, F. 1118 (Mal)  
 — with — & Cantrell, 205 (Mal)  
 Huffaker C. B. with Ray & Soto (816) (Mal)  
 — Soto, H. & Ray H. 39\* (Mal)  
 Hughes, C. O. with Brackett, 15 (Mal)  
 Hughes, W. 661 766 767 1062 (Def. Dis)  
 Hulse, W. 640 (Dem)  
 Hall, R. Lovell, B. J. Openshaw H. T. Pavman, L. C. & Todd A. R. (822) (Mal)  
 Hammelen, L. R. 355 (Hel)  
 Humphrey, A. A. 415 (Am)  
 — with Munk, Zimmerman & Maner 958 (Misc Dis)  
 Hundley J. M. & Seabell, W. H., 1061 (Def. Dis)  
 Hunt, A. H. 1040 (Am)  
 Hunter E. A. 861 (Misc Dis)  
 Hunter G. W. with Faust, Wright & McMillan, 758 (Hel)  
 — with Warren, V. G. & Warren, J. 1056 (Hel)  
 — Waller T. H. & Jahnes, W. G., J. 788 (Ent)  
 — & Worth, C. B. 567 (Hel)  
 Hunter T. A. & 293 (Mal)  
 Huntriss, R. L., with Peters & Porter (346) (Hel)  
 Husman, C. N. with Jones, Lundquist & Decker (628) (Mal)  
 — with Lundquist, Madden & Travis, 785 (Ent)  
 Hutchinson, J. H. Pyppard, J. S. & Gloose-White, M. H. 338 (R F)  
 Huyck, J. H. with Stanbury (257) (Ent)  
 Hyler G. with Karamchandani, 848 (Sp)  
 Hyman, A. S. 155 (Misc Dis)  
 Hynd R. S. 448 (R F)  
 Hynes, M. Ishaq M. & Morris, T. L., 473 (Haem)

L

Iams A. M. Tenen M. M. & Flanagan H. F.  
 587 (Der)  
 Iaracci V. with Mosto 63 (Der)  
 Ibarra Pérez R. & González Prendes M. A.  
 561 (Is) 563 933 (Lep)  
 — with — 226 (Lep)  
 d Ignazio C. 1042 (R.F.) 1130 (Typh.)  
 — & Codelconcini E. 73 1130 1131  
 (Typh.) 1012 (R.I.)  
 Imbrosciano G. 732 (Typh.)  
 Imperial Chemical (Pharmaceuticals) Limi-  
 ted 1010 (Mal)  
 India 72 968 (Reports etc.) 81 (B.R.)  
 Indian Med. Gaz. 822 (Mal)  
 Indian Research Fund Association 129 130  
 131 bis (Chl)  
 Ingle L. with Kearns & Metcalf 681 (Ent)  
 Ingraham H. S. with Zarafonetta & Berry  
 746 (R.F.)  
 Innes J. with Fenton 298 (Mal)  
 International Labour Review 1082 (Reports  
 etc.)  
 Ionesco-Mihaiesti C. & Cruca M. 321  
 (Typh.)  
 Inarrie D. R. 1128 (Leish.)  
 Irigoyen Ramirez A. with Romeo Viamonte  
 (197) (Mal)  
 Irons, F. N. 734 (Typh.)  
 — & Arnbrust C. A. Jr 550 (Typh.)  
 Irons J. V. Topping N. H. Shepard C. C.  
 & Cox H. R. 924 (Typh.)  
 Isaac F. 652 (Am)  
 Isaq M. with Hynes & Morris 475 (Haem.)  
 Israels M. C. G. with Wilkinson & Fletcher  
 1065 (Haem.)

J

Jackson C. H. N. 312, 420 (Tryp)  
 Jackson E. B. with Smadel & Rights 547  
 919 (Typh.)  
 Jackson W. P. U. 1169 (Der)  
 Jacobs H. R. 206 (Mal)  
 Jacoby H. 1167 (Misc. Dis.)  
 Jaffe E. with Moore Kessel Simonsen,  
 Marmorston Llewellyn, Kaplan Golden &  
 Anderson, (650) (Dys)  
 Jaffé R. 350 (Hel.)  
 Jahn F. with Johnson & Trussell, 67 (Prot)  
 Jahnke W. G. Jr with Hunter & Weller  
 783 (Ent.)  
 Jailer J. W. 11 (Mal)  
 Jalili M. with Halawany 540 (Leish.)  
 James S. P. 783 (Misc. Dis.)  
 Jansen G. 938 (Hel.)  
 Jaquet Del Pozo G. (935) (Lep)  
 Jarcho S. 3 (Mal)  
 Jarvis J. F. 224 (R.F.)  
 Jayawickreme S. H. 868 (Ent)  
 — & Viles W. J. 1079 (Ent.)  
 Jeffery G. M. with Metcalf, Hess Smith &  
 Ludwig 102 (Mal)  
 Johnson W. L. 31 (Typh.)  
 — with Mackie Davis Fuller Knapp  
 Steenacker Stager Traub Millsbaugh,  
 Austrian Bell Kohls Wei Hal & Graham  
 917 (Typh.)

Jennings G. H. 623 (Mal)  
 Jencensus H. 971 (B.R.)  
 Johnson A. S. Jr & Berry M. G. 351  
 (Hel)  
 Johnson B. C. Mitchell, H. H. & Hamilton  
 T. S. 591 (Heat Str)  
 — with Shields Hamilton & Mitchell 591  
 (Heat Str)  
 Johnson, C. M. with Shrapnel & Sandground  
 928 (Am.)  
 Johnson D. H. & Wharton G. W. 640  
 (Typh.)  
 Johnson G. Trussell M. & Jahn F. 67  
 (Prot)  
 — with — (254) (Prot)  
 Johnson H. A. & Eason J. L. Jr 1111  
 (Mal)  
 — with Parker 13 (Mal)  
 Johnson H. C. with Darby & Jones 687  
 770 (Sp)  
 Johnson H. N. 184 (Mal)  
 Johnson J. A. Jr Martin W. B. & Breslow  
 I. 645 (Den)  
 Johnson M. B. & Damon S. R. 915 (Typh.)  
 Johnson M. S. 78 (Reports etc.)  
 Johnstone I. L. 1183 (Oph)  
 Joki E. with Glaver & Rovick (1064)  
 (Reports etc.)  
 Jones E. with Darby 949 (Sp)  
 — with — & Johnson, 667 770 (Sp)  
 Jones E. R. with Bell, (1123) (Tryp)  
 Jones H. A. with Deoner 531 (Mal)  
 — Burrell R. W. & Knupling E. F.,  
 530 (Mal)  
 — with — Maple Hinchey & Elde 101  
 (Mal)  
 — Landquist A. W. Deonier C. C. &  
 Hasman, C. N. (628) (Mal)  
 — with — Travis Madden & Schroeder  
 159 (Ent)  
 Jones J. with Dobes 672 (Der)  
 Jones R. with Hendelberger Mayer Alving,  
 Cruise Pullman & Whorton, 1013 (Mal)  
 Jorg. M. E. with Mazza & Miyara, 208  
 (Tryp)  
 Jorge J. M. & Re P. M. (1048) (Hel.)  
 Jorner L. with Fulton, 435 (Typh.)  
 Jorner L. with Fulton, 435 (Typh.)  
 Jorner O. F. 265 (B.R.)  
 Jorner Sun, C. (721) (Leish.)  
 Jorner E. with Notestein (281) (Reports,  
 etc.)

K.

Kalandadze L. P. & Sagatova, I. S. 1106  
 (Mal)  
 Kalmbach, E. R. 331 (Pl)  
 Kamel A. 1128 (Leish.) 1154 (Hel)  
 Kane C. A. with Most London Laricetes,  
 Schroeder & Hayman 1011 (Mal)  
 Kan Hsu-Chieh, (236) (Mal)  
 Kaplan A. 296 (Mal)

- Kap. F with Moore Kessel, Smonsen  
 Marmontson Llewellyn Golden Anderson  
 & Jaffe. (850) (Dys)  
 K. Rha L I Reid H S & Becker F T  
 1110 (Mal)  
 Kaplan V & Gluck A C 438 (A F)  
 Karamchandani P V & Hyder G 948 (Sp)  
 Kark S L & Kark E 162 (Reports etc)  
 Kark W 559 (Am) 780 (H at Str)  
 Karmann G with Vranes & Baer (670)  
 (Vim)  
 Karmahv K I 802 (Prot)  
 Kartman L 740 (M) 780 (Hel)  
 — Campau L J Newcomb I H &  
 Morrison F D 716 (Troph)  
 Katrelenboorn I (897) (Misc Dns)  
 Kato C L Jr with Lippard 538 (Mal)  
 Kauer C L with Timpert 45 (A)  
 Kaufman C with Kott & Coope 749  
 (RT)  
 Kautz W H 1196 (Reports, etc)  
 Kay H B with Wappler 29 Typh)  
 Keen B H 867 (Reports etc)  
 — & Grocott R C 168 (Prot)  
 — & Tocher H A 1189 (Misc Dns)  
 — & Miller W C 567 (Misc Dns)  
 Kearns C W Ingle L & Mcintosh R L 681  
 (Ent)  
 Kerle A. D 1063 (Sp)  
 — & Bond J I 563 (Sp)  
 Keener G G Jr 197 (Mal)  
 Kest H with Bechelli & Roitberg 235 (Lep)  
 Kevak A 783 (Misc Dns)  
 — with Cullman Watts & Tman 942  
 (Def Dns)  
 Kelsey F E with Oldham H (Mal)  
 — & Gehrig E M A 404 (Mal)  
 — Cantrell W & Geising E M K  
 (625) (Mal)  
 Kesamora, B with Tschyrs 743 (Am)  
 Kemev M 364 (Ent)  
 Kern F Jr 42 (Am)  
 Kershaw W F 857 (Am)  
 Kerran P with Catanes 247 (Der)  
 — with Lafrou Loooux & La Ponce 854  
 (Chi)  
 Kessel J F with Moore Smonsen Mar  
 montson, Llewellyn, Kaplan, Golden  
 Anderson & Jaffe (850) (Dys)  
 Kess, A with Michelson & Caster 1081  
 (Def Dns)  
 Khamallah, A with Hitt 1137 (Dns)  
 Khalil Bey M Halwan A & Gamal Nor  
 El Deen 50 (Hel)  
 Kharatun, E M with Alpatov & Nastukova,  
 69 (Ent)  
 Kibbe F W with Lewis 304 (Mal)  
 Kierland R R Sheard C Mason H L &  
 Lobitz, W C 1008 (Mal)  
 Kiker C C & Spurrman, R F 309 (Mal)  
 King E. J., Gilchrist, M & Tarnok A L  
 707 (Mal)  
 — Wootton, I D P & Gilchrist M 822  
 (Mal)  
 King L S with Davis & Harrell (143) (Hel)  
 King H with Andrews & Walker 427 794  
 (Typh)  
 King, J D with Adams Macgrath  
 Townshend, Da ey & Harvard 406\* (Mal)
- King, J D with Adams & Townshend 400  
 (Mal)  
 — with Macgrath Adams, Harvard &  
 Millet 238 (Sp)  
 — with — Totter Rugby &  
 Shaddon, 821 (Mal)  
 — with — Townshend Da ey &  
 Harvard 406\* (Mal)  
 King W D & Sebrell W H 854 (Def.  
 Dns)  
 Kinserv F R with Herbet 850 (Misc.  
 Dns)  
 Kirby H 222 (Am) 254 (Prot)  
 Kirby Smith H T 148 (Vms)  
 Kirk R & Lewis D J 796 1185 (Ent)  
 Kirk R L with Gunn & Waterhouse, 507  
 (Reports etc)  
 Korman B D 944 (Def Dns)  
 Kuskaddon R M & Renshaw R J F 168  
 (Prot)  
 Ktchen S F with Boyd 104 1003 (Mal)  
 — & Sadler G G 416 (BI)  
 Kloeberg J 303 (Mal)  
 Klem E F with Browning Raphael &  
 C Biens, 648 (Typh)  
 Klem H S 120 (Typh)  
 Klemm F A 259 (Reports etc)  
 Kligman A M with Vedman 778 (Der)  
 Kline B S with Snowingroth, 300 (Hel)  
 Klingensmith C W 648 (P)  
 Knapp J A with Macine, Da is, Fuller  
 Strinacker Stager Traub, Jefferson,  
 Milbrunish Austman Bell, Kohls, Wei Hal  
 & Conham 917 (Typh)  
 Knight, A L with Belkin & Roseboom, 8  
 (Mal)  
 — with Roseboom 817 (Mal)  
 Knipe F W 1181 (Ent)  
 Knipping E F 443 (Ent)  
 — with Jones Deener & Burrell 530  
 (Mal)  
 — with Lindquist Madden & Wilson 150  
 (Ft)  
 — with Madden & Lindquist 158 (Ent)  
 — with Eliot T S & Bloch, E. H.,  
 631 (Mal)  
 Knowley M H Eliot T S & Bloch, T S &  
 Stratman-Thomas, W H Eliot, T S &  
 Bloch, E. H 1113 (Mal)  
 Knoll E W & Howell, A M 444 (Am)  
 Knott J with Caridin, 248 (Der)  
 Knowles, F L & Fink, J W., 529 (Mal)  
 — & Smith C S 710 (Mal)  
 Knox W E 1005 (Mal)  
 Koch M B with Spies, Lopez, Monodides &  
 Munich 474 (Sp)  
 — with — Milanec Monodides &  
 Munich 780 (Sp)  
 — with — Vilter & Caldwell, 376  
 (Haem)  
 — with Vilter & Spies 375 (Haem)  
 Koch W 594 (Heat Str)  
 Kochman A with Anzian Chubkova  
 & Anzian, 13 (Mal)  
 Koeningfeld E C H 101 (Rab)  
 Koepfle J B with Mead Rappport, Sencer &  
 Ma hard 623 (Mal)  
 Koepfle, J A with Rummreich 429 (Typh)  
 Kohls C M with Blake Marcy Sadnak &  
 Bell 327 (Typh)

Hohls with Cooley 864 (Ent)  
 — with Mackle Davis Fuller Knapp  
 Steinsacker Stager Traub Jefferson  
 Willspaugh Austrian, Bell Wei Hsu &  
 Gurnham 917 (Typh)  
 — with Philip 119 (Typh)  
 Kojenikov P V 724 (Lesh)  
 Kopicowska L with Silva 428 (Typh)  
 Kordy M I with Halawan (1143) (Am)  
 Kornblineth W with Feigenbaum 1074  
 (Misc Dis)  
 Krakower C Hoffman W A & Artmayer  
 J H 227 (Hel)  
 Krapcho J with English Clark Shepherd  
 Mason & Roblin (903) (Mal)  
 Kraus H. 869 (BR)  
 Kringelbach J with Frandsen 1163 (Sp)  
 Krishnan B G Ramchandran S &  
 Sadhu K 473 (Def Dis)  
 Kruse C W & Cartrell F E (308) (Mal)  
 — & Metcalf R L 1111 (Mal)  
 Kuller S W with Harvey & Tredway 490  
 (Misc Dis)  
 Kuitunen Ekbaum E 940 (Hel)  
 Kumm H W Osborne-Mesa E & Bonhell  
 Manrique J 599 (Ent)  
 Kutznok A with Olutski Olelnuk &  
 Czaczek (635) (Typh)  
 Kuzmina L A with Pavlovsky 744 (R F)  
 Kuznetsov B with Bobnaskoy & Karyakin  
 268 (BR)  
 Kuzvakin A with Bobnaskoy & Kuznetsov  
 268 (BR)  
 Kwoh C S (288) (Mal)  
 Kykor G C Cornatzer W E. & McEwen  
 M M. 706 (Mal)

## L

Lacas C. da S (488) (Der)  
 Lackov J B & Steink M L 794 (Ent)  
 Ladell W S S 250 675 (Heat Str)  
 Laemmert H W Jr 644 (S F)  
 — & de Castro Ferreira, L 33 (Y F)  
 Lagodsky H. with Lannoy (1025) bis (Tryp)  
 Lagos Nigeria, 838 (Y F)  
 Laha, P N 9 (394) (Mal)  
 Lahiri M N 137 bis (R F)  
 Lahnun W H. 741 (Pl)  
 Laigret J & Corcos A. 739 (Don)  
 Lairet F Jr 437 (Y F)  
 de LaJude P with Floch, 342 833 (Lep)  
 352 (852) 1155 (Hel) 704 (Mal) 908  
 (Tryp)  
 Lambert J D 203 (Mal)  
 Lampton R S with Gilje (444) (Am)  
 Lamy L. 442, 743 (Am)  
 — with Deschamps (352) (Hel)  
 Lancet, 416 (Bl) 485 (Der)  
 Landsborough, D (1158) (Hel)  
 Lane J D with Binford 487 (Der)  
 Lane W F with Day & Wood (853) (Hel)  
 Ling, S 43 (Am)  
 Lange K & Matzner M J 1109 (Mal)  
 Laptev A A 50 (Hel)  
 Larcher V & Romana C 110 (Tryp)  
 Laramas, M with León & Beltrán 1017 (Mal)  
 Larnon E. B. & Thomson V 1194 (Ent)  
 Larrh J E Jr (351) 739 bis (Hel)

Lasch W. with Gruenfelder 1148 (Lep)  
 Lasser E. P & Cassinelli J F 567 (Hel)  
 Latif V & El Kordy M I (1158) (Hel)  
 Latshev N I 602 (Ent)  
 Laube P J with Yang 661 (Hel)  
 Lannoy L 314 423 424 (Tryp)  
 — & Lagodsky H (1025) bis (Tryp)  
 Laurent A. with Florio Hammon & Stewart  
 737 (Don)  
 Laus F with Ramos 909 (Tryp)  
 Lauterburg Boujoor M (494) (Ent)  
 Laver G & Stefanopoulos G 463 (Hel)  
 Lavietes P H. with Most London Kane  
 Schroeder & Hayman 1011 (Mal)  
 Lavoipierre M with de Meillon (160) (Ent)  
 Lawless D K 651 (Am)  
 Lawrence E. A. with Abbey 627 (Mal)  
 — & Bennett R E. 36 (Dys)  
 Lawton A. H. with Ashburn Perrin &  
 Brady 662 (Hel)  
 — Brady F J Ness A T & Haskins  
 W T 65 (Hel)  
 League of Nations 268 (BR)  
 Lehned B. with Wanson 1191 (Ent)  
 Le Chulton F (625) (Mal)  
 — & Berge C 915 (Typh)  
 Leckoe M W with Browning Calver &  
 Walls 633 (Tryp)  
 Leo R K C & Pang H O 66 (Misc Dis)  
 Leede W E & Josey A I 573 (Hel)  
 Lefrou G Kervran P Loudoux V & Le  
 Poncin N 554 (Chl)  
 Le Gac P 213 916 bis (917) (Typh)  
 — & Bergeix L (327) (Typh)  
 — Sente P & Combescot de Marsaguet  
 G 621 (Mal)  
 Le Gall R. 284 (Mal)  
 Lehmann G D & Prenderville J T 787  
 (Prot)  
 Leishman A W D 366 (Sp)  
 Lentko J S 1127 (Lesh)  
 Lestman, M Z 1139 (Am)  
 — & Vitalukaya, I A. 1143 (Am)  
 Lestner A J 381 (Misc Dis)  
 Lendrum A C. with Fisher 1186 (Misc Dis)  
 Lengauer L 459 (Lep)  
 Leunhoff L. with van den Ende Locket  
 Hargreaves & Niven 918 (Typh)  
 León A P 731 (Typh)  
 — Beltrán E. & Laramas M R 1017  
 (Mal)  
 — & Cano C 731 (Typh)  
 Leon, L A 1059 (Hel)  
 Leon Blanco F with Oteiza 587 (Der)  
 Leon y Blanco F & Sanchez Garcia, E. 588  
 (Der)  
 Leonova V A 748 (R F)  
 — with Sofev 744 (R F)  
 Le Poncin V with Lefrou Kervran &  
 Loudoux 554 (Chl)  
 Leprosy Review 461 (Lep)  
 Lerner E. M 1031 (Lab)  
 Le Roy with Martin Sureau Babooet &  
 Bodcart 464 (Hel)  
 Lesbe A. with Silverman 39 (Am)  
 Levaditi, J C. & Panther R 731 (Typh)  
 Levi-Castillo R. (7) (Mal)  
 Levine A. C. with Gottfried 301 (Mal)  
 Levy B. M 150 (Der)

- Lewillon R. 208 (Tryp)  
 — with an Hoo! Henard Peel & Rodjesterakv 538 (Tryp)  
 Lewis, B. O. with Soderman, 135 (Am)  
 Lewis, D. J. with Kirk, 798 1193 (Ent)  
 Lewis Medical Scientific & Technical Library 270 (B R)  
 Lewis, R. A. & Kibbe F. W. 304 (Mal)  
 — with Senelke 320 (Lesh) 877 (Prot)  
 Liberman C. with Augustine 570 (Hel)  
 Lids T. with Tomulty Nichols & Singewald 819 (Mal)  
 Liebermann H. R. 334 (Am)  
 Lieber H. with Vollmer 201 (Mal)  
 Liem S. D. A. an Thiel P. H. 719 (Tryp)  
 Lier & Schneider B. (939) (Hel)  
 Likoff W. 1133 (T ph)  
 Lilbe R. D. 603 (Lab)  
 Lima L. de S. & Cerqueira, G. de C. 47 226 (Lep)  
 Lindberg, D. O. \ with Bayler & Baggenstons, (567) (Misc Dis)  
 Lindquist A. & McDuffie V. C. 795 (Ent)  
 Lindquist A. V. with Gahan 99 (Mal)  
 — with — & Tra 89 (Mal)  
 — with — & Norton 99 (Mal)  
 — with Jones Deonier & Hosman (923) (Mal)  
 — Madden A. H. Hosman, C. V. & Trava B. V. 795 (Ent)  
 — with — & Burpliss 155 (Ent)  
 — Wilson H. G. & Kurling E. F. 159 (Ent)  
 — with Schroeder 963 (Ent)  
 — Trava, B. V. Madden A. H. Schroeder H. O. & Jones H. A. 159 (Ent)  
 — Wilson H. G. Schroeder H. O. & Madden A. H. 160 (Ent)  
 Lindsay A. with Bovernick & Heffernan, 824 825 (Mal)  
 Lindsay S. F. 796 (Misc Dis)  
 Lindskog G. E. & Walters, V. 1140 (Am)  
 Lipman M. O. with Rose & Culbertson 232 (Hel)  
 Lippert, V. W. & Haer G. L. Jr. 328 (Mal)  
 Lippincott S. W. with Elbertson Cateno Gordon & Marble 608 (Mal)  
 — Hemelbrock, W. B. Carroo C. C. & Marble A. 1009 (Mal)  
 — — Gordon H. H. Gotthelb L. & Marble V. 823 (Mal)  
 — with Goodman Wenberger Marble & Wright, 573 (Hel)  
 — with Gordon, Marble Engstrom & Brunning 1007 (Mal)  
 Litchfield J. T. Jr. with Marshall & White 826 (Mal)  
 Little P. A. & Subbarow V. 523 (Tryp)  
 Liu W. T., with Snyder & Zarakosets, 428 (Tryp)  
 Liu, Y., with Tan, 333 (Am)  
 Livadas G. A. (1015) (Mal)  
 Lively H. R. with Pollard, Wilson & Woodland 736 925 (Den)  
 Llewellyn H. with Moore, Hessel Smooren, Marmorestein, Kaplan, Golden Anderson & Jaffe (680) (Dys)  
 Lobetz W. C., with Kierland, Sheard & Mason, 1009 (Mal)  
 Lobo, R. 608 (Hel)  
 Locket, S. 417 (81)  
 — with van den Ende Hargreaves rec & Lennhoff 918 (Tryp)  
 Loeb P. with Richardson Walker & Miller 440 (R F)  
 Loeb R. F. 708 (Mal)  
 Loeffler W. with Mosser 843 (Tryp)  
 Lofgren R. & Soule M. H. 335 (445) (R F)  
 London I. M. with Most, Kane Lavette Schroeder & Ha man 1011 (Mal)  
 Lopes C. F. 562 (Ys)  
 Loper G. G. with Spees, Menendez Munich & Koch, 474 (Sp)  
 López Fernández J. with Talco 112 (Tryp)  
 Lopez Toca, R. with Spees Frommeyer Garcia Lopez & Gwiner 949 (Sp)  
 Loranger G. L. with Woodward & Philip 536 (Tryp)  
 Lorentz P. H. 117 (Tryp)  
 Loudoux, S. with Lefron, Kervran & Lo Poncin, 564 (Chi)  
 Lounie E. M. with Collier 1126 (Lesh)  
 — with Williamson 845 (R F)  
 Lovell, B. J. with Hull Openshaw Payman & Todd (822) (Mal)  
 Lovibond J. L. 1040 (Am)  
 Low G. C. 317 (Lesh) 783 (Misc Dis)  
 Lowe J. 523 (Mal) 540 (Lesh) (807) (Reports etc.), 1129 (Tryp)  
 — with Das Gupta & Chakravarti, 288 (Mal)  
 Lomado Morales, A. 205 (Mal)  
 Lucas R. B. 651 (Am)  
 Lockesh, M. Taylor A. H. Cole H. D. & Goldmann, T. 678 (Heat Str)  
 Ludwig G. W. with Metcalf Hess Smith & J. Sery 10\* (Mal)  
 Lupaca, G. (617) (Mal)  
 Lusk, J. W., 426 (Tryp)  
 Luthra, P. V. 1184 (Uk)  
 Lwoff M. Boet, D. & Funke, A. 313 (Tryp)  
 — & Nicole P. (1029) (Tryp)  
 Lyman F. E. with Price 14 (Mal)

## M.

- Macan, T. T. 203 (Mal)  
 MacArthur J. V. 1009 (Mal)  
 MacArthur W. (909) (Mal)  
 MacArthur W. P. 602 (Ent)  
 McCall, h. B. with Cooperman, Elshajen & Ruegamer 772 (Haen)  
 MacCallum, P. O. with Buckland, Dudgeon, Edward Henderson Begg, Wren, Rowlands & an den Ende Bergmann Curtis & Shepherd 436 (Tryp)  
 MacCallum, W. P., 516 (Mal)  
 McCarthy D. D. with Dock, 680 (Hel)  
 Macchia olo, A. 647 (Pi)  
 — & Cafuntes, O. 23 (Tryp)  
 — & Ovale, H., 1032, 1033 (Tryp)  
 — & Ovale H. 1033 (Tryp)  
 McCollum, W. T. with Fruchtman 493 (Misc Dis)  
 McCoy O. R. 1073 (Misc Dis)  
 McCubagh, Mich., 783 (Misc Dis)  
 McCulloch, R. V. 1034 (Tryp)

- McDaniel F L. White B. V. Jr & Thompson C M 1060 (Def Dis)  
 Macdonald G 684 (Reports etc.)  
 McDonald S. 183 (Rab.)  
 McDuffie W. C. with Lindquist 785 (Ent.)  
 McEwen M M with Kyler & Cornatzer 706 (Mal)  
 McGovern V 30 (Typh.)  
 McGowan E. R. Falce J H & Goodhue L D 962 (Ent.)  
 Macgregor I 1138 (Dys.)  
 McIntosh, D G with Brodie Cook & Drysdale, 841 (Dys.)  
 Mack A. G with Sulabeger Addenbrooke Joyce & Greenberg, 1168 (Der.)  
 Mackay Dick J 128 (Pl.)  
 Mackie T T *et al* 1182 (Typh.)  
 — Davis G E Feller H S. Knapp J A. Steinacker M L. Stager K. E. Traub R. Jellison W L. Millsapach, D D. Anstrian R C. Bell E. J. Kohle G M. Wei Ha & Graham J A V 917 (Typh.)  
 McKibbin J M with Williamson Hegsted & Stare 1009 (Mal.)  
 McKinney W W with Robinson, 293 (Mal.)  
 Mackinnon J E with Talce 292 (Mal.)  
 Mackinnon P G with Moyne Stubbs Crowdy Citrine Blacklock, Engledow & Henderson 70 (Reports etc.)  
 Mackworth N H 1071 (Heat Str.)  
 Macleod J with Crauford Benson 638 (Typh.)  
 McLachle J L 1022 (Tryp.)  
 MacLough A. C. with Brumpt, 835 (Typh.)  
 McLishon M. C. with Wayson 648 (Pl.)  
 McLartin W J 231 (Hel.)  
 McMullen D B & Beaver P C. 138 (Hel.)  
 — with Faust, Wright & Hunter 756 (Hel.)  
 McNaught J B (355) (382) (Hel.)  
 McNaught, W W 391 (Mal.)  
 Madden, A. H. with Lindquist, Husman & Travis 795 (Ent.)  
 — & Knippling, E. F. 158 (Ent.)  
 — with — Travis Schroeder & Jones, 159 (Ent.)  
 — with — Wilson & Knippling 169 (Ent.)  
 — with — & Schroeder 159 (Ent.)  
 Madonavelita, J 1011 (Mal.)  
 Macgranth, B. G *et al* 99 bis 416 905 (Mal) 553 (Y.F.)  
 — Adams A. R. D. Havard R. E. King J D & Millet R. F. 238 (Sp.)  
 — King J D. Tottley M. M. Rugby D J & Shadden R. A. 821 (Mal.)  
 — Townshead R. H. Davey T H & Havard R. E. 402 (Mal.)  
 — with — & — 402 (Mal.)  
 — with Spinks & Tottley (707) (Mal.)  
 Magalhães B. F & Freire S. A. (1123) (Tryp.)  
 Magath, T B. & Mathieson D R. 350 753 756 (Hel.)  
 Magnuson H. J with Schatz Wakeman & Eagle 1025 (Tryp.)  
 Magoon E. H. 877 (B.R.)  
 Magron E. 926 (Pl.)  
 — & Brisou J 928 (Pl.)  
 Magy H. I & Hoskins W M 601 (Ent.)  
 Mahaffy A. F with Smithburn 34 (Y F)  
 Mahfouz M. with Amin & Sherif 43 (Am.)  
 Major F W with Barber & Wragg (1011) (Mal.)  
 Majumder A R. Bagchi A K. & Ghosh, B K. 441 (Dys.)  
 Makari J G 823 (Mal.)  
 Malanga C with Seeler & Pierson 309 (Mal.)  
 Malbrant R with Parrot, (160) (Ent.)  
 Malcolmson M E with Craigie Watson & Clark, 814 (Typh.)  
 Maldonado J F 1143 (Am.)  
 Maldonado Capriles J (1185) (Ent.)  
 Malo-Juvera F with Ortiz Manotte & Payne 324 (Typh.)  
 Mandekos A. G. 906 (Mal.)  
 Mandelstam J with Gullman & Gullman 668 (Def. Dis.)  
 Maner G D with Mirck Zimmerman & Humphrey 858 (Misc. Dis.)  
 Manson-Bahr P 317 (Lemh.) 607 (B.R.) 684 688 1189 1200 (Reports etc.) 783 1072 (After Dis.)  
 Manson-Bahr P E. C. & Charters A. D 1186 (Misc. Dis.)  
 Manson J M S 1202 (Reports etc.)  
 Manuwa S L A 782 (Ulc.)  
 Maxwell, R. D 485 (Lab.)  
 Maple J D with Deonier Barrell & Cochran 101 (Mal.)  
 — with — Jones Hinchey & Eide 101 (Mal.)  
 Mara, L. 1078 (Ent.)  
 Marble A. with Ellerbrook, Lippincott Cateso & Gordon 628 (Mal.)  
 — with Goodman Weinberger Lippincott & Wright 573 (Hel.)  
 — with Gordon Engstrom, Brunsting & Lippincott 1007 (Mal.)  
 — with Lippincott, Ellerbrook Hesselbrock & Carrico 1009 (Mal.)  
 — with — — — Gordon & Gottlieb 523 (Mal.)  
 Mariani Tomatti, G 49 (Hel.)  
 Mariano J 48 (Lep.)  
 Marshall F G & Alary L. (354) (Hel.)  
 Mario S (324) (Mal.)  
 Markowitz J 741 (Chl.)  
 Markson J L & Dawson J 12 (Mal.)  
 Marlingens Mille with Montal & Brun, Mille. 454 (Lep.)  
 Marmarston J with Moore Kessel, Simonsen Llewellyn Kaplan, Golden, Anderson & Jaffe (650) (Dys.)  
 Marnette H. with Sautet (258) (Reports etc.) 482 (Hel.)  
 Marple C. D (377) (Der.)  
 Marques A P with Bancroft, Guinto & Rodriguez 454 (Lep.)  
 Marray A. M. & Philpotts G C. L. (136) (Am.)  
 Marshall E. L. Jr (905) (Mal.)  
 — with Dearborn, 404 (Mal.)  
 — Litchfield J T & White H. J 828 (Mal.)

- Marshall P B 15 97 (Mal)  
 — with Goodwin, J B (Tryp)  
 — & Rogers, E W 93 (Mal)  
 Mason H L W with English, Clark Shop-  
 Lord Knappe & Roblin (905) (Mal)  
 Martin R Le Roy Sureau B Badouet, P  
 & Parnet, N 484 (Hel)  
 — with Parnet (901) (Ent)  
 Martin W B 669 (Vms)  
 — with Johnson & Brendow 645 (Don)  
 Martinier Ruez M & Villuana A 747 (R F)  
 Martins A V 776 b (Vms)  
 — & Versiani A (904) (Mal)  
 — with — & Sobrinho 754 (Hel)  
 — — & T penambé A A 718 *dis*  
 (Tryp)  
 Marzabini G M 38 (Am) 45 (R F)  
 Marvin, H N & Rydoo R H 715 (Mal)  
 Ma on, R L with Kierland Sheard &  
 Lobitz, 1004 (Mal)  
 Mason P H Daniels W B Paddock F K  
 & Gordon H H 1157 (Hel)  
 Matheson D R with Magath, 350 755  
 756 (Hel)  
 Mathur W A Goyal R 17 (Fl)  
 Matzner M J with Lange 1106 (Mal)  
 Maury R F with Blake Sadusk Kohle &  
 Bell, 347 (Typh)  
 Maer J H 156 (Misc Dns)  
 Mayer M with Heidelberg M ung  
 Crause Jones, Pullman & Whorton, 1013  
 (Mal)  
 Mayer M M with Heidelberg & Coates  
 1013 (Mal)  
 — with — & Demarest 816 (Mal)  
 Mayer R L & Brocasen D 1125 (Tryp)  
 Maynard J T with Mead, Rapport, Senear  
 & Koepf 823 (Mal)  
 Mazza, S 631 (Tryp)  
 — Basso C & Basso R 720 909 (Tryp)  
 — Miyara S & Jorg M E 206 (Tryp)  
 Mazzotti L 137 (Hel)  
 — & Ochoa, M T 472 (Hel)  
 — & Varela, G 1135 (Typh)  
 Mbeppé J with Chaboul 1122 (Tryp)  
 Mead J F Rapport, M V Senear A E  
 Maynard J T & Koepf, J B 823 (Mal)  
 Meares A R R 498 (Reports etc)  
 Mehus R 1127 (Loush)  
 Medical Advisory Division Headquarters  
 Supreme Allied Command S E Asia, 203  
 (Mal)  
 Medical J Australia 529 (Mal)  
 Megaw J 603 (Reports etc)  
 de Meillon V & Daniels D H S 868 (Ent)  
 — & Lavoipierre M (180) (Ent)  
 de Meira, B T V with da Cruz Ferreira, 683  
 (Ent)  
 — Guizo, J & Costa A de M F (780)  
 (Hel)  
 Meloney H E (223) (Am)  
 — with Zuckerman 223 (Am)  
 Mellanby K 1132 (Tryp)  
 Mello, G B with Caney 797 (Mal)  
 de Mello J P (827) (Mal)  
 de Mello R P with Cruz, 660 (Hel)  
 Melillo A R Wilson, D B Glasgow J P  
 & Hocking, L S 87 (Mal)  
 Mendell T H 548 (Typh)  
 Mendelsohn H V 673 (Der)  
 Mendez T H with Del Pozo & Gaudier  
 (148) (Vms)  
 Menéndez A with Spies Milanes Koch &  
 Minnich 769 (Sp)  
 Menéndez J A with Spies, Lopez Minnich &  
 Koch 474 (Sp)  
 Menon, I G K 595 868 (Misc Dns)  
 Menon, T B & Veluth, G D (297) (Mal)  
 Merganser J C 405 (Mal)  
 Mermo C 552 (Bart)  
 Merrill D with Rubenstein & Shulman 292  
 (Mal)  
 Mersley C & Daskind E 932 (Haem)  
 Mersky C (483) (Misc)  
 Mertens E 257 (Lab)  
 Microbeans L with Cusick, (210) (Typh)  
 — with — Badensky Franko &  
 Muntzmann (210) (Typh)  
 — with — Muntzmann & Paras-  
 chivescu (210) (Typh)  
 Metcalf R L 193, 363 (Mal)  
 — Hess A D Smith, G E Jeffery  
 G M & Ludwig G W 107 (Mal)  
 — with Kearns & Ingle 681 (Ent)  
 — with Kraus 1111 (Mal)  
 de Menlaestre J with Vmcke Parent &  
 Bertheau 291 (Mal)  
 Meyer May J with Ho-Dac Di Vu-Dinh-  
 Tung Tung-That Tung & Dinh Van-  
 Thang 87 (B R)  
 Meyersberg H A 59 (Def Dns)  
 Michael P 53 (Hel)  
 Michelson I C with O'Donovan 1175  
 (Oph)  
 Michener C D 797 963 (Ent)  
 Michelson, O Carter, W O & Keys A  
 1061 (Def Dns)  
 Milanes, I with Spies, Menéndez Koch &  
 Minnich, 769 (Sp)  
 Miles V I (199) (Mal)  
 Millan Gutierrez J 1123 (Loush)  
 Miller E S & Beeson, P B 732 (Typh)  
 Miller H with Moseley 318 (Tryp)  
 Miller I with Richardson, Walker & Loeb  
 446 (R F)  
 Miller J F with Whittier & Elnhorn, 577  
 (Hel)  
 Miller S E 49 (Hel)  
 Miller W C with Kean & Tucker 597  
 (Misc Dns)  
 Millet, R F with Macgrath, Adams  
 Haard & Kunz 138 (Sp)  
 Mills W G 348 (Hel)  
 Milupa gh D D with Macno Davis  
 Fuller Knapp Steenacker Stager Traub  
 Jellison, Anstran, Bell, Kohle Wei Hel &  
 Gusham 917 (Typh)  
 Milosovicova, E N 1063 (Mal)  
 Milvinsky H 583 (Hel)  
 Minnich, V with Spies Lopez Menéndez &  
 Koch 474 (Sp)  
 — with — Milanes, Menéndez & Koch,  
 769 (Sp)  
 Minton J 1175 (Oph)  
 Mirck G S Zimmerman, H M Maner  
 G D & Humphrey A A 958 (Misc  
 Dns)  
 Mischel A. (827) (Mal)

- Mitchell H. H. with Johnson & Hamilton 591 (Heat Str)  
 — with Shields Johnson & Hamilton 591 (Heat Str)  
 — with Specter & Hamilton (378) 591 bis (Heat Str)  
 Mitchell J. P. 78 (Reports etc.)  
 Mitra S. K., (857) Der.  
 Mitra, S. N. with Bose Ghosh & Datta 1028 (Leish.)  
 Miyara S. with Mazza & Jörg 208 (Tryp.)  
 Mohan B. N. 187 (Mal.)  
 Mohanty, J. K. 137 (R.F.) 250 (Ulc.) (380) (Misc. Dis.)  
 Mohr W. 406 408 (Mal.)  
 Mohun A. F. 866 (Lab.)  
 Motter B. 454 (Lep.)  
 Moll, A. 505 (B.R.)  
 Mollaret P. & Diego R. (853) (R.F.)  
 Mom, A. M. & Basombiro G. 455 (Lep.)  
 Monchadsky A. with Blagoveshensky & Bregetova, (160) (Ent.)  
 Mondor 87 (B.R.)  
 Monsanto Chemical Company 648 (Pl.)  
 Montel M. L. R. 503 (B.R.)  
 Montel R. 344 1152 bis (Lep.) 449 450 (1s.)  
 — & Bassot, (342) (Lep.)  
 — Brun, Mlle & Mariangeas Mlle 454 (Lep.)  
 Monteny V. A. R. 1060 (Def. Dis.)  
 Montézin G. with Funke & Bovet 713 (Mal.)  
 Moore C. V. Bierbaum O. S. Welch A. D. & Wright 477 (Haem.)  
 Moore D. F. 1180 (Oph.)  
 Moore F. J. Kosak J. F. Simonsen D. G. & Farmington J. with Llewellyn H. Kaplan F. Golden F. Anderson N. & Jaffe, E. (850) (Dys.)  
 Moore J. A. Young M. D. Hardman N. H. & Stubbs T. H. 1002 (Mal.)  
 — with — Stubbs Ehrman, Hardman Ellis & Burgess 5 (Mal.)  
 Moore L. D. 4 (Mal.)  
 Moore M. & Ackerman L. V. 857 (Der.)  
 Mooser H. 611 (B.R.)  
 — & Löffler W. 543 (Typh.)  
 Morales A. L. 634 (Leish.)  
 Morales F. H. 837 (Typh.)  
 — with Oliver-Gonzalez 471 (Hel.)  
 Moreau P. & Ouary G. 378 (Ulc.)  
 Morey M. with Sprea 768 (Def. Dis.)  
 Morgan C. N. 1040 (Am.)  
 Mornet J. with Parrot & Cadenat (160) (Ent.)  
 Mornet P. with Parrot & Cadenat (602) (Ent.)  
 Morris R. S. 537 (Tryp.)  
 Morris T. L. with Hynes & Ishaq 475 (Haem.)  
 Morrison F. D. with Hartman Campau & Newcomb 716 (Tryp.)  
 Mornassey G. C. & Derrick E. H. 31 (Typh.)  
 Morton F. A. with Gahan Travis & Lindquist 99 (Mal.)  
 — with Snyder 1198 (Ent.)  
 Mowley V. & Miller H. 318 (Tryp.)  
 Moss E. S. with Burns & Broeck 468 (Der.)  
 Most H. with Birnkant & Greenberg, 231 (Am.)  
 — & Hayman J. W. Jr 1004 1005 (Mal.)  
 — London I. M. Hane C. A. Lavietes, P. H. Schroeder E. F. & Hayman J. M. Jr 1011 (Mal.)  
 Mosto D. & Iancu V. 63 (Der.)  
 Mottouille L. (1202) (Reports etc.)  
 Moulder J. W. & Evans E. A. Jr 1118 (Mal.)  
 — with Speck & Evans 1118 (Mal.)  
 Moulton, F. R. 881 (B.R.)  
 Mourão B. M. 585 (Der.)  
 Moustardier G. with Cornil & Poursines 216 (Pl.)  
 Movno Stubbs R. E. Crowdy R. E. Citrine W. Mackinnon P. G. Blacklock, M. G. Engleadow F. L. & Henderson, H. D. 79 (Reports etc.)  
 Mugrage F. R. with Florio & Stewart 438 (Den.)  
 Muir E. 458 654 (Lep.)  
 — with Rogers, 689 (B.R.)  
 Mukerjee S. 1030 (Leish.)  
 Mukerji A. K. & Sen Gupta K. K. 230 (Hel.)  
 Mukerji B. 1012 (Mal.)  
 — with Dutta & Sekar 1029 (Leish.)  
 Muller H. E. with Chernock 968 (Lab.)  
 Mullett C. F. (196) (Rab.)  
 Munteanu G. with Cruca Mesrobian Badenski & Franke (210) Typh.)  
 — with — & Paraschivescu (210) (Typh.)  
 Munter E. J. & Packham A. 721 (Leish.)  
 Murgatroyd F. 1040 (Am.)  
 Murphy R. C. Jr & Shapiro S. 581 (Haem.)  
 Murray E. S. with Ecke Gilliam Snyder Yeomans & Zaratonets 545 (Typh.)  
 — with Yeomans Snyder Ecke & Zaratonets 636 (Typh.)  
 — with Zaratonets, Ecke Yeomans & Snyder 912 (Typh.)  
 — & Snyder J. C. 433 (Typh.)  
 — with — & — 822 (Typh.)  
 Muspratt, J. 704 (1000) (Mal.)  
 Muselman M. M. 664 685 (Def. Dis.)  
 Mowat E. M. K. 747 (R.F.)  
 — with Trowell 143 363 (Def. Dis.)  
 N  
 Naftalin J. M. with Bookless 199 (Mal.)  
 Nagley L. 296 (Mal.)  
 Nail S. K. with Soman 439 (Chl.)  
 Nájera Angulo L. 721 (Leish.)  
 — 447 (R.F.) (647) (Den.) 1026 1027 bis (Leish.)  
 Nájera, L. 284 (Mal.) (317) (Tryp.) 832 (Leish.)  
 Napier L. E. 10 (Mal.) 77 884 (Reports etc.) 783 (Misc. Dis.) 867 (B.R.)  
 Nashed E. (1184) (Oph.)  
 Nastukova O. K. with Alpatov & Khartuluri, 69 (Ent.)  
 Nath T. 1184 (Ulc.)  
 Naval Medical Research Institute and U.S. Naval Hospital (1157) (Hel.)  
 Navar S. L. with Badhwar & Chopra 672 (Der.)



- Neel R. (313) (Tryp)  
 Neff F C, with Davis 779 (Der)  
 Nephmo R. A 577 (Hel)  
 Nelson, A. A with Pittsburgh, Calvery &  
 Glassman, 525 (Mal)  
 Nelson, E. C & Bayliss M 1046 (Hel)  
 Nelson J W 535 (Tryp)  
 Nelson L M 303 (Mal)  
 Nerv Guimarães, F., 381 (Prot)  
 Newbitt, H H J (864) (Ent)  
 Ness A T with Lawton Brady & Haskins,  
 85 (Hel)  
 Nettel F R 233 (Hel)  
 Newjean, G 189 (Rab) 324 (Tryp)  
 News A 1150 (Lep)  
 Neuvi Lemaire M 1086 (B R)  
 Newcomb E. H with Kartman, Campen &  
 Morrison, 718 (Tryp)  
 Newman, P P (853) (Lep)  
 Newton, W L & Pratt, I 6<sup>5</sup> (Hel)  
 ——— Wright, W H & Pratt I 52 (Hel)  
 Nichols, F with Tinnally Sengwald &  
 Lutz 819 (Mal)  
 Nichols L 185 (B R) 1082 (Def Dis)  
 Nicolle P with La H (1028) (Tryp)  
 Niles W J with Javencikretic 1079  
 (Ent)  
 Nilo F with Tazara & Bonagosa 487  
 (Der)  
 Nilo F L (227) (Hel) 583 (Der)  
 ——— & Fernandez J C (257) (Ent)  
 Nisbet T W 481 (Der)  
 Nith, F Cooge M & Kaufmann, G 749  
 (R.F.)  
 Niven, J., with van den Ende Locket,  
 Hargreaves & Leenhoff, 916 (Tryp)  
 Niven, J S F with Buckland, Dodgson,  
 Edward Henderson-Begg MacCallum,  
 Rowlands & van den Ende with Bangmann,  
 Curtis & Shepherd 436 (Tryp)  
 Nixon W C W., with Eckstein, 623 (Mal)  
 Noad, K B 1132 (Tryp)  
 Noble, B G 1034 (Reports etc)  
 Nobrega G 846 (R.F.)  
 Noe W L J, Greene C C Jr & Cheney  
 G 521 (Mal)  
 Nor-el Daz, G with Halkwant, 1109 (Mal)  
 (1145) (Ya) (1156) (Hel)  
 ——— with ——— & Awn, 114 (Am)  
 Norman-Walker J N 1039 (B R)  
 Noronha, A J (3) (Mal)  
 Norris L C with Robertson Daniel,  
 Farmer & Heuser 1006 (Haem)  
 \*Norstrom F W & Jurkat E (261)  
 (Reports, etc)  
 norovich, G G 955 (Der)  
 Nubes Andrade R. 674 (Der)  
 Nyka, W 119 (Tryp)

## O.

- Quarler E. G. & Fidler H K., 1029 (Leish)  
 Ockuly E A 227 (Hel)  
 O'Connor J L., 642 (Tryp)  
 O'Donovan, W J & Michaelson, I C 1175  
 (Oph)  
 Ogden, F N with Zucizer 950 (Haem)  
 Ogden, L W., with Rees 857 (Heart Str)  
 Ogilvie W H., 251 (Misc. Dis.)

- Ozham F K & Kelsey F E., 11 (Mal)  
 ——— with ——— Cantrell & Geising (825)  
 (Mal)  
 ——— with ——— & Geising 404 (Mal)  
 Olenik E. with Ohtaki Craschke &  
 Katsenok, (635) (Tryp)  
 Ohtaki, L Olenik, E. Craschke J W &  
 Katsenok A. (635) (Tryp)  
 Oliveira E. de S 940 (Hel)  
 Oliver Gonzalez, J 357 (Hel)  
 ——— Baggi N & Rivera Ledn, J 347 (Hel)  
 ——— with Culbertson & Rose 54 354 763  
 (Hel)  
 ——— with Hernandez Morales, 1158 (Hel)  
 ——— with ——— & Pratt, 1045 (Hel)  
 ——— & Morales, F H 471 (Hel)  
 ——— & Pratt C K 348 (Hel)  
 Oliveira Nava, B 753 (Hel)  
 Olmos Castro N & Bonath, A A 849 (Lep)  
 ——— with ——— 850 (Lep)  
 Olson, T A & Dahms R G (796) (Ent)  
 Omar M with Wolman & Abu-Taleb 338  
 (R.F.)  
 Openshaw H T with Hall, Lovell, Payman  
 & Todd, (822) (Mal)  
 Orkin, J M 501 (Reports etc)  
 Orlov P M, with Beljennashev & Shikova,  
 1112 (Mal)  
 Orta L F with Goldman, 664 (Hel)  
 Orus Mariotto C with Bustamante &  
 Varela, 1134 (Tryp)  
 ——— Malo-Juvora, F & Payne G C., 324  
 (Tryp)  
 Osborn, S H 867 (Reports, etc)  
 Osborn-Moss, E with Kumm & Boasell-  
 Magnoque 569 (Ent)  
 Osgood S B 92 (Mal)  
 Osman, A A 417 (B)  
 Osorio M T with Mazzotti, 472 (Hel)  
 Ostrowsky V G 1142 (Am)  
 Otenta, A & Leon Bianco F 587 (Der)  
 Ott, W H with Seeler 413 (Mal)  
 Ouary G with Moreau, 378 (Uic)  
 Ovalle H with Macchavello 1033 (Tryp)  
 ——— with ——— & Cifuentes, 1032, 1033  
 (Tryp)  
 Owen E C (822) (Mal)  
 ——— with Card Davis, Rose & Tsey (1110)  
 (Mal)  
 Owen, W B 6 (Mal)  
 Owens B B with Curtis 486 (Der)  
 Ortuck, M H 157 (Misc. Dis.)

## P.

- Pacheco-Lima, R. 1150 (Hel)  
 Packham, A 723 (1027) (Leish)  
 ——— with Munter 721 (Leish)  
 Packer H 1108 (Mal)  
 Paddock, F H with Mason, Daniels &  
 Gordon 1157 (Hel)  
 Padilla, E with Golden, 1185 (Uic)  
 Page A R P Stringer A & Blackith, R E.  
 600 (Ent)  
 Page J A 1060 (Def Dis)  
 Pal R. 515 (Mal)  
 Palley A & Brummer T., 1083 (Reports, etc.)  
 Palmer E D 796 (Ent)  
 Pampuna, E 875 (B R)

- Pang H Q with Lee 66 (Misc. Dis.)  
 Pang K. H. 325 (Typh.)  
 — Zia, S. H. Chen S. M. & Feng Y. S. 326 (Typh.)  
 Panja, D. with Ghosh (490) (Misc.)  
 Panja, G. 218 (Chl.) 219 (Dys.) 378 (Ulc.) (1127) (Leish.)  
 — & Ghosh, S. K. 218 (Chl.)  
 — with Gupta & Chatterjee 1138 (Pl.)  
 Panther R. with Levaditi 731 (Typh.)  
 Papafagos T. (904) (Mal.)  
 Paré M. 1169 (Der.)  
 Paraense L. 309 (Mal.)  
 Parachivescu, N. with Craca Mesrobianu Badenski & Munteanu (210) (Typh.)  
 Parent M. with Vincke 307 (Mal.)  
 — with — Berteaux & de Meulenaere 291 (Mal.)  
 Park R. G. 64 (Heat Str.)  
 Parker R. C. & Hollender A. J. 186 (Rab.)  
 Parker W. V. & Johnson H. A. 13 (Mal.)  
 Parkos J. with Cooke Elkes, Fraser & Peenoy 946 (Sp.)  
 Parrot G. 328 (Typh.)  
 Parrot, L. & Malbrant R. (160) (Ent.)  
 — & Martin R. (601) (Ent.)  
 — Vornet J. & Cadenat J. (160) (602) (Ent.)  
 — with Sergeant & Donatien (603) (Ent.)  
 Parry E. 624 (Mal.)  
 Parry T. E. with Tattersall 430 (Typh.)  
 Pascalo H. 969 (Reports etc.)  
 — & Cruz E. 546 (Typh.)  
 Pasoyro P. (376) (Haem.)  
 Patel J. C. 220 221 (Am.)  
 Paul, B. M., with Gupta Chatterjee & Ghose 130 (Chl.)  
 de Paula Souza G. H. 128 1135 (V. F.)  
 Pavillard S. S. 489 (Misc. Dis.)  
 Pavlovskii, E. N. & Skramnik, A. N. 223 (R.F.)  
 Pavlovsky E. N. 65 (Misc. Dis.) 743 (R.F.)  
 — & Karmolina I. A. 744 (R.F.)  
 Payman L. C. with Hull Lovell Openshaw & Todd (822) (Mal.)  
 Payne G. C. with Ortiz-Mariotte & Malojuvera 324 (Typh.)  
 Pecoreau V. with Carboni & Rodolfo Mercau 847 (Lep.)  
 Peddie J. J. G. with Cottrell 333 (Am.)  
 Peel, E. & Chardome M. 1159 (Hel.)  
 — with van Hoof Lewillon, Heurard & Rodjstvensky 636 (Tryp.)  
 — with Wanson & Heurard 253 (Hel.)  
 Peenoy A. L. P. with Cooke Elkes Fraser & Parkos 946 (Sp.)  
 Pepper D. S. with Elson & Forrester 559 (Dys.)  
 Pepper O. H. P. & Díaz Rivera R. S. 356 (Hel.)  
 Pereira, A. C. 1151 (Lep.)  
 Pereira O. de L. 609 (B.R.)  
 Pereira P. C. R. 584 (Lep.)  
 Pérez A. & Romafia, C. 112 (Tryp.)  
 Pérez Ara A. & Pérez Viguera L. 580 (Hel.)  
 Pérez Viguera I. with Pérez Ara, 580 (Hel.)  
 Perret-Gentil, A. 96 200 (Mal.)  
 Perrin T. L. with Ashburn Brady & Lawton 682 (Hel.)  
 Perry D. J. with Spies Cogswell & Frommeyer 60 (Def. Dis.)  
 Perves M. (524) (Mal.)  
 Peset Alexandre T. & Romeo Viamonte J. M. (196) (Mal.)  
 Pessoa S. B. & Amaral D. F. 43 (Am.)  
 — & Barretto M. P. 1030 1127 1128 (Leish.)  
 Peters C. V. Huntress R. L. & Porter J. E. (346) (Hel.)  
 Peters J. T. 246 (Der.) 534 (Bl.)  
 Pfanner E. F. 674 (Der.)  
 Philip C. B. 554 (Den.)  
 — & Kohls G. M. 119 (Typh.)  
 — Woodward T. E. & Sullivan R. R. 733 (Typh.)  
 — with — & Loranger 836 (Typh.)  
 Philip M. I. Ramakrishna V. & Rao V. V. 203 (Mal.)  
 Phillips G. C. L. with Murray (136) (Am.)  
 Picard H. & Benson, T. 42 (Am.)  
 Piers F. (1084) (Reports etc.)  
 Pierson J. with Seeler & Mahanga, 309 (Mal.)  
 Pike J. B. with Taft 447 (R.F.)  
 Piney A. & Hamilton Paterson, J. L. 870 (B.R.)  
 Pinkerton H. with Graff 22 (Typh.)  
 — with Settle & Corbett 27 (Typh.)  
 Pinto C. 163 (Reports etc.)  
 — with Torres, 658, 1156 (Hel.)  
 Pinto H. (1027) (Leish.)  
 Pinto M. R. with de Azevedo & Cambournac, (716) 828 (829) (Tryp.)  
 Pippard J. S. with Hutchinson & Gleason White 338 (R.F.)  
 Prot, R. & Bourgain, M. 336 337 bis (R.F.)  
 Prittar C. A. 1178 (Oph.)  
 Prittingh, C. S. with Downs, 1001 (Mal.)  
 Planchart, M. A. with Sanabria, 156 (Misc. Dis.)  
 Platt B. S. 362 (Def. Dis.)  
 Plant, A. 1190 (Prot.)  
 Plesson, M. (853) (Hel.)  
 Plotner K. 393 (Mal.)  
 Plots H. with Bell 434 (Typh.)  
 — Bennett B. L. & Reagan R. L. 920 (Typh.)  
 — & Wertman K. 429 (Typh.)  
 — & Bennett B. L. 725 (Typh.)  
 Podlesker A. 13 (Mal.)  
 Pogge R. C. 456 (Lep.)  
 — with Favet 343 460 (Lep.)  
 Polak, M. F. 264 (B.R.)  
 Pollard M. with Davis 1033 (Typh.)  
 — Livsey H. R. Wilson, D. J. & Woodland J. C. 738 825 (Den.)  
 Polson A. Joubert, F. J. & Haig D. A., (954) (Vms.)  
 Polunordvinov A. D. 283 (Mal.)  
 Pondé A. with Barreto (424) (Tryp.)  
 Ponder E. 61 (Haem.)  
 Porter J. E. with Peters & Huntress (346) (Hel.)  
 Porto A. with Rocha e Silva & Andrade 1052 (Hel.)  
 Portugal H. & Rocha G. L. 1148 (Lep.)  
 Poeschl H. 268 (B.R.)  
 Post-Graduate Med. J. (830) (Hel.)  
 Potter C. & Guilham E. M. 1193 (Ent.)

- Pouran, J. with Cooml & Monstardier 216 (M)  
 Power S 677 (Misc Dis)  
 Pownall, R. F. 334 (Ent)  
 Prazm 1 880 (B.R.)  
 Prabhu M. V. 683 (Lep)  
 Pratt, C. K. 470 (Hel)  
 — with Hernandez Morales & Ohler  
 Gonzalez 1045 (Hel)  
 — with Ohler Gonzalez 348 (Hel)  
 Prait, I. with Newton 52 (Hel)  
 — with — & Wright 53 (Hel)  
 Prendville J. T. with Lehmann 787 (Prot)  
 Preme with v. Bormann 324 (Typh)  
 Price M. V. & Lyman F. E. 14 (Mal)  
 Proc Roy Soc Med 835 (Typh) 944 (Def.  
 Dis) 1040 (Am)  
 Prokopenko L. I. & 300 701 (Mal)  
 Prost P. with Farinaud (285) (Mal)  
 Prout, C. with Heidelberg Hmdle & Rose  
 1013 (Mal)  
 Prudhomme R. O. 857 (Lep)  
 Pug Solana M. Fontes A. & Antonio  
 Queros, J. 784 (Hel)  
 Pullar E. M. (1048) (Hel)  
 Pullen, R. L. with Stuart, 836 (Typh)  
 Pullman, T. V. with Heidelberg Mayer  
 Alving, Craige Jones & Whorton 1013  
 (Mal)  
 Pustom, V. 264 (B.R.)  
 Putnam, P. with Russell & Rao 106 (Mal)  
 Pyles W. J. with Gellhorn van Dyke &  
 Topolova, 722 (Lesh)

## Q

- Queen, F. B. with Sweeney & Friedlander  
 114 (Lesh)  
 Quarter F. 144 (Def Dis)

## R

- Rabom, C. (705) (Mal)  
 Radford, C. D. 683 (Ent)  
 Radna, R. 1041 (Am) 1146 (Lep)  
 Raetig, H. 124 211 (Typh)  
 Raffaele G. 1016 (Mal)  
 Rafay, A. 1144 (R.F.)  
 Rai Chandhuri M. V. with Chandhuri, 843  
 (844) (Am)  
 Ranson, C. C. (822) (Mal)  
 Rakshit, P. C. with Bose & Ghosh 928 (Dys)  
 Ramachandran S. with Arshinan & Sadhu  
 473 (Def Dis)  
 Ramakrishna, V. with Phalep & Rao 203  
 (Mal)  
 Ramez J. J. & Laus F. J. A. 909 (Tryp)  
 Randolph, N. M. (1123) (Tryp) 1145 (R.F.)  
 Rangam C. M. with Reddy 444 (Am)  
 Rao S. S. 231 (Hel)  
 Rao T. R. 519 (Mal)  
 — with Russell & Putnam 106 (Mal)  
 Rao V. G. 1073 (Misc Dis)  
 Rao V. V. with Philp & Ramakrishna 203  
 (Mal)  
 Raper A. B., Wilson M. E. & Wilson D. B.  
 6 (Mal)  
 Raphael, M., with Browning, Klen &  
 Coblenz, 548 (Typh)

- Rappaport, F. & Eschhorn F. (1184) (Haem)  
 Rapoport, M. M. with Mead, Senear Maynard  
 & Koepfla 823 (Mal)  
 Ratcliffe A. W. 967 (Lab)  
 Ray J. C. with Ghosh, H. & Ghosh, N. V.  
 1125 (Lesh)  
 Re, P. M. with Jorge 1048 (Hel)  
 Read, H. S. with Kaplan & Becker 1116  
 (Mal)  
 Reegan, R. L. with Plotz & Bennett, 820  
 (Typh)  
 Reardon, L. V. with Rees, 556 (Am)  
 Reddy D. G. & Rangam C. M. 444 (Am)  
 — & Thangavelu M. 495 (Lab)  
 Rees C. W. & Reardon, L. V. 556 (Am)  
 Rees W. H. & Ogden, L. W. 857 (Heat Str)  
 Rees, C. R. with Cooper & Beard, 1027  
 (Lesh)  
 — with Dwindelle Stenberg & Sheldon,  
 1043 (As)  
 Remond I. M. & Webb F. R. 531 (Def  
 Dis)  
 Renhart, J. B. with Harrell, Wolff &  
 Venning, 823 (Typh)  
 Remlinger P. (196) (Rab)  
 Reabourn, E. T. 857 (Heat Str)  
 Reagle S. with Gast Galva 113 (Lesh)  
 Renshaw R. J. F. with Kalladon, 158  
 (Prot)  
 Reppert, L. B. with Wright & Cutting 781  
 (Heat Str)  
 Resmer R. with Rodham 444 (Tryp)  
 Rev Pathologic et Med Trop (307) (Mal)  
 Revista Brasileira d Leprosia 451 (Lep)  
 Rey H. with Hoffaker & Soto 392 (Mal)  
 — Soto, H. & Hoffaker C. B., (816) (Mal)  
 Rhodessa, Southern, 1201 (Reports etc.)  
 Ribbards C. R. 409 621 904 1014 (Mal)  
 Ricci, M. (832) (Hel)  
 Rich, W. M., with Danney Browning, 568  
 (Oph)  
 Richardson, A. P. Walker H. A. Loeb P. &  
 Miller I. 446 (R.F.)  
 Richardson, D. N. (822) (Mal)  
 Richardson, D. T. 680 (B.R.)  
 Richet, C. (116) (Typh)  
 Richter C. P., 331 (Pi)  
 Ridley H. 85 (Hel) 834 1018 (Tryp) 588  
 (Oph)  
 Roemerichand G. 48 (Heat Str)  
 Rifkin, H. Celada, E. B. Zarrow M.  
 Henderson, D. G. & Whitehead, J. O.  
 183 (Rab)  
 — & Thompson, K. J. 353 (Hel)  
 — with — & Zarrow 469 (Hel)  
 — with Zarrow 571 (Hel)  
 Rigby D. J. with Macgrath, Adams, King,  
 Totty & Stadden, 621 (Mal)  
 Ripdon, R. H. 715 1116 (Mal)  
 — with Marvin 715 (Mal)  
 — with Rostorfer 309 (Mal)  
 — & Rodwell, H. Jr 310 (Mal)  
 — & Varnadoe N. B. 630 (Mal)  
 Rights F. L., with Smadel & Jackson, 547  
 619 (Typh)  
 Rigler H. 116 (Typh)  
 Riley R. L. with Goodline, 962 (Ent)  
 Rissman, J. E. F. with Freedberg, 243  
 (Am)

- Rivera León J. with Oliver González & Biaggi 347 (Hel.)  
 Robertson, E. I. Daniel L. J. Farmer F. A. Norris L. C. & Heuser G. F. (1936) (Haem.)  
 Robinson, G. 243 (Haem.)  
 Robinson, H. M. Jr. & McKinnay W. W. 233 (Mal.)  
 Roblin R. O. Jr. with English Clark Shepherd Watson & Krapcho (1903) (Mal.)  
 Roca-García, M. with Bates 32 323 (A. I.)  
 Rocha G. L. with Portugal 1148 (Lep.)  
 Rocha e Silva M. & Graña R. 1052 bis (Hel.)  
 — Porto A. & Andrade S. O. 1052 (Hel.)  
 Rodhain J. (1903) (Tryp.)  
 — & Reissler R. 424 (Tryp.)  
 Rodjestyensky B. with van Hoof Lewinlon Hennard & Peel 536 (Tryp.)  
 Rodolfo Mercau A. with Carboni & Pecoraro 847 (Lep.)  
 Rodriguez H. H. 183 (Rab.)  
 Rodriguez J. N. with Bancroft, Guinto & Marques 454 (Lep.)  
 — with Doull Guinto & Bancroft, 453 (Lep.)  
 Rodriguez Molina, R. 239 (241) (Sp.)  
 Rodriguez Pascual C. (1935) (Lep.)  
 Rogan J. M. & Coombes A. E. R. 824 (Mal.)  
 Roger H. (229) (Hel.)  
 Rogers A. M. & Dammala G. J. 1049 (Hel.)  
 Rogers E. W. with Marshall 88 (Mal.)  
 Rogers H. B. 302 (Mal.) 1081 (Lab.)  
 Rogers, L. 1153 (Lep.)  
 — & Malir E. 639 (B.R.)  
 Romaña, C. 111 (Tryp.)  
 — with Larcher 110 (Tryp.)  
 — with Pérez 112 (Tryp.)  
 — & Terracini E. 110 (110) (Tryp.)  
 Romeiro, O. dos S. (1123) (Tryp.)  
 Romeo B. J. 1133 (Typh.)  
 Romeo Viamonte J. M. 817 (Mal.)  
 — & Irigoyen Ramirez A. (197) (Mal.)  
 — with Poet Alexandre (196) (Mal.)  
 Romero H. with Viel, 545 (Typh.)  
 Romijn, C. 1164 (Haem.)  
 Ronch P. R. with Cluver & Jokl (1034) (Reports, etc.)  
 Rose A. S. with Heidelberger Prout & Hindle 1013 (Mal.)  
 Rose F. L. with Bastford & Curd (1110) (Mal.)  
 — with Curd (822 bis) (1110) (Mal.)  
 — with — Davis Owen & Tucey (1110) (Mal.)  
 — with — & Davey 394 400 (Mal.)  
 Rose H. M. Culbertson J. T. & Lipman, M. O. 232 (Hel.)  
 — with — & Oliver-Gonzalez 54 354 783 (Hel.)  
 — Duane R. B. & Fischel, E. E. 433 (Typh.)  
 Rosenbaum, S. 147 (Haem.)  
 Rosenthal J. 1069 (Der.)  
 Rostorfer H. H. & Rugdon R. H. 309 (Mal.)  
 Rotberg A. with Bechelli & Keil, 225 (Lep.)  
 Roth H. 359 (Hel.)  
 Rotman, C. M. H. 34 (Pl.)  
 Roebaud E. (290) (Mal.) 419 (Tryp.)  
 — & Caubot P. 418 (Tryp.)  
 — & Colas-Belcour J. 383 (Ent.)  
 — Stefanopoulou G. J. & Duvalon S. 311e 419 (Tryp.)  
 Rouvier J. with Despujols Bergeret & Calmet (253) (Misc. Dis.)  
 Row R. 1147 (Lep.)  
 Rowe H. P. 79 (Reports etc.)  
 Rowlands, J. S. F. with Buckland Dudgeon Edward Henderson Reg. MacCallum Victor Rowlands & van den Ende with Bargmann Curtis & Shepherd 436 (Typh.)  
 Roy B. C. 725 (Typh.)  
 Roy D. N. 871 (B.R.)  
 Roy Nav. Med. Bull. 244 (Vms.)  
 Rozeboom L. L. with Belkin & Knight 6 (Mal.)  
 — & Knight & L. 817 (Mal.)  
 Rubenstein A. D. Shalman, M. H. & Merrill D. 292 (Mal.)  
 Rubin S. S. (543) (Typh.)  
 Rudmell H. Jr. with Rugdon 310 (Mal.)  
 Rudra M. N. & Bhattacharya K. P. 787 (Misc. Dis.)  
 Ruegger W. R. with Cooperman & Elvehjem (1067) (Haem.)  
 — with — & McCall, 772 (Haem.)  
 Rugiem H. R. & Cohen, J. 326 (Typh.)  
 Ruiz Costero G. with Hernández Morales (228) (Hel.)  
 Rumreich, A. S. & Koepke J. A. 429 (Typh.)  
 — & Wynn, R. 35 (Pl.)  
 Ruppel, A. 202 (Mal.)  
 Ruabcliffe 85 (B. R.)  
 Russell, J. C. with Eyles & Sabrosky 190 (Mal.)  
 Russell P. F. (620) (Mal.)  
 — Rao T. R. & Putnam P. 196 (Mal.)
- 3.
- de Sá J. M. with Gama, 936 (Hel.)  
 Sabrosky C. W. with Eyles & Russell 199 (Mal.)  
 Sachs A. 729 (Typh.)  
 Sadhu K. with Krishnaiah & Ramachandran 473 (Def. Dis.)  
 Sadler G. G. with Kitchin 416 (B.L.)  
 Saduk, J. F. Jr. with Blake, Maacy Hobbs & Bell 327 (Typh.)  
 Sagatolova I. S. with Kalandadze 1106 (Mal.)  
 Sagber F. 1023 (Lesh.)  
 — with Dostrovsky 1030 (Lesh.)  
 Salgado P. with Convit Azulay & Bermudez 457 (Lep.)  
 Sanabria, A. & Planchart M. A. 156 (Misc. Dis.)  
 Sanchez Garcia E. with Leon y Blanco 586 (Der.)  
 Sanderson G. with Adams, 396 (misc. Mal.)  
 Sandground J. H. with Shrapnel & Johnson, 828 (Am.)  
 Sandler A., 1037 (Den.)  
 Sangster C. B. 759 (Hel.)  
 — & Ray H. B. 29 (Typh.)  
 Sanjay S. C. (1180) (Misc. Dis.)

- Saphir W. 34 (Hel) 377 (Heat Str)  
 Sardana, M N 1182 (Oph)  
 Sasse, S with Wilson & Down, (952)  
 (Haem)  
 Sasportas L 282 (Mal)  
 Satti, M H with Horgan, 17 (Leish)  
 Santot, J & Audibert, Y 780 (Ent)  
 — & Marnette H (268) (Reports etc)  
 482 (Hel)  
 Savino E 36 (Pl)  
 Saxton, W J Hatcher F & Derrick, E H  
 1169 (Der)  
 Sayre, M H P 1192 (Typh)  
 Scadding J G 132 (Dys)  
 Schaafsma, A with Grasset & Hodgson, 670  
 (Nms)  
 Schiller K H 210 (Typh)  
 Schallek W with Welsh, (1090) (Ent)  
 Scharrif J W 203 (Mal)  
 — with White S 203 (Mal)  
 Schatz A Magnuson H & Wakeman S A  
 & Layle H 1025 (Trip)  
 Schene H G 1178 (Oph)  
 Schenck I M with Blankenhorn, Viter &  
 Austin, 945 (Def Dis)  
 Schenkman, E L with Freund Thomson  
 Sommer & Walker 311 (Mal)  
 Scherzer C 374 (Haem)  
 Schloesser R J 575 (Hel)  
 Schmidt, W 117 (Typh)  
 Schmitt, C L Alpus, O & Chambers G  
 482 (Der)  
 Schneider M 1170 (Oph)  
 Schneider R with Leger (936) (Hel)  
 Schoetter M with Deynat & Gille-Semel,  
 330 (Pl)  
 Schofield A L with Wolfe 782 (Hel)  
 Schofield K with Simpson, (825) (Mal)  
 Schonbrunner E 118 (Typh)  
 Schorr S with Drackman 133 (Am)  
 Schroeder E F with Most, London, Kans,  
 La retes & Hayman, 1011 (Mal)  
 Schroeder H O & Lindquist A W 983  
 (Ent)  
 — with — Travis Madden & Jones 169  
 (Ent)  
 — with — Wilson & Madden, 169 (Ent)  
 Schuffner W 233 (Hel)  
 Schaffer W A P with Swellengrabel,  
 (355) (Hel)  
 Schuchardt, V T & Hemphill, E C 748  
 (R I)  
 Schujman, S 846 1152 (Lep)  
 Schultes W 169 (Mal)  
 Scott H 917 (Leish)  
 Scott, H H 880 (B R)  
 Scott J A 463 1050 (Hel) (909) (Reports  
 etc)  
 Seal S. C. 17 (Chl)  
 — with Sen 880 (Def Dis)  
 Sobrell, W H with Handley 1061 (Def  
 Dis)  
 — with King 854 (Def. Dis)  
 Soelar A O Malanga, C & Pearson, J 309  
 (Mal)  
 — & Ott, W H 412 (Mal)  
 Schult, R (67) (Misc Dis)  
 Sarte P with La Gac & Combescot de  
 Maragnat, 821 (Mal)
- Seiler C C with Dutta & Mukerji 1028  
 (Leish)  
 Seiser L with Sharnoff & Gelger 1002  
 (Mal)  
 Sen, A K 953 (Haem)  
 Sen, K & Ghose N 576 (Hel)  
 Sen, P C with Seal S C 880 (Def. Dis)  
 Sen, R L with Das Gupta, 1145 (R F)  
 Sen Gupta, K K with Mukerji 230 (Hel)  
 Sen Gupta, P C 425 722 (Leish)  
 — with Bose & Bose 219 (Dys)  
 — & Chakravarty N K 833 834 (Leish)  
 Senour A E with Mead Rapport Maynard  
 & Koopff, 823 (Mal)  
 Senekye H A & Lewis R A 320 (Leish)  
 677 (Prot)  
 Sergeant, E 500 (R F)  
 — Donatien, A & Parrot, L. (903) (Ent)  
 Sergeant, Et 148 (Vma)  
 Sethadrisathan, N 251 (Ulc)  
 Settle E B Pinkerton, H & Corbett, A. J  
 27 (Typh)  
 Settemio Lacon, 903 ses (Mal)  
 Shah, M A 1173 (Oph)  
 Shallenberger P L with Ginsberg, 1007  
 (Mal)  
 Shapiro S with Murphy 881 (Haem)  
 Sharnoff J G. Genger J & Seiser I 1002  
 (Mal)  
 Shear M J with Topping & Bengtson, 18  
 (Typh)  
 Shourd C with Kierland Mason & Lobitz,  
 1006 (Mal)  
 Sheehan H L 238 (R F)  
 Sheldon A J with Dwindelle Rem &  
 Sternberg 1043 (Y)  
 Shelley W B & Hinrichs, S M 875 (Heat  
 Str.)  
 Shepard, C. C. 21 (Typh)  
 — with Leone Topping & Cox, 924 (Typh)  
 — & Topping N H 21 735 (Typh)  
 — with — 910 911 (Typh)  
 — & Wyckoff R W G 913 (Typh)  
 Shepherd M A, with Buckland, Dudgeon,  
 Edward, Henderson-Begg MacCullum,  
 Niron, Rowlandy van den Ende Berg-  
 mann & Curtis, 438 (Typh)  
 Shepherd, M M 782 (Ulc)  
 Shepherd R G with English, Clark,  
 Maroon, Knapcho & Robin (906) (Mal)  
 Sherif, M A F with Amin & Mahfouz 43  
 (Am)  
 Shields J B Johnson, B C Hamilton, T S  
 & Mitchell H H 591 (Heat Str)  
 Sherris, D 706 (Mal)  
 Shih La Chang 37 222 (Am)  
 Shroton, J C with Breslow Walker Yost &  
 Hauser (406) (Mal)  
 Shlenova, M F with Beklemishev & Orlov  
 1112 (Mal)  
 Shlimovitz N 780 (Lep)  
 — with Wartman, 1003 (Mal)  
 Shortt, H E 217 (Leish) 684 (Reports, etc.)  
 1132 (Typh)  
 Shoukn, Y S 118 (Typh)  
 Shoune, K L 482 (Misc)  
 Shrapnel, B C Johnson C. M & Sandground  
 J H 928 (Am)  
 Shrivastava, D L with Hhatnagar 840 (Pl)

- Shropshire G with Laughlin & Howser (157)  
(Misc. Dis.)
- Shulman, M. H. with Rubenstein & Merrill  
292 (Mal.)
- Shumeko A. I. 48 (Hel.)
- Shuto P. G. 8 (393) (Mal.)
- Siccé A. 257 (Reports etc.)
- Siddons L. B. with Das Gupta 4 (Mal.)
- Silber R. H. with Edison & Tennent 363  
(Def. Dis.)
- Silva R. & Kopsiowska 423 (Typh.)
- da Silva E. M. 668 (Haem.)
- da Silva, P. B. 1158 (Hel.)
- da Silva Lacar C. (151) (Der.)
- de Silva S. 40 443 (Am.)
- Silverman D. & Leslie A. 39 (Am.)
- Simmons E. L. with Talarferro & Talarferro  
629 (Mal.)
- Simmons J. S. Whayne T. F. Anderson,  
G. W. Horack H. M. & collaborators 86  
(B.R.)
- Simmons S. W. et al. 104 (Mal.) 789 (Ent.)  
— with Fay & Clapp 790 (Ent.)  
— with Silerli & Tarzwell 792 (Ent.)  
— with Upholt Games & Arnold 794  
(Ent.)
- Simões J. M. P. with Cambournac 95 306  
(Mal.)
- Simonin P. & Girard J. (478) (Haem.)
- Simonsen D. G. with Moore Kessel,  
Marmorston, Llewellyn Kaplan Golden  
Anderson & Jaffe (650) (Dys.)
- Simpson J. 944 (Def. Dis.)
- Simpson J. C. E. & Schofield K. (625) (Mal.)
- Singewald M. L. with Tumulty Nichols &  
Lidz 819 (Mal.)
- Singh, B. 238 (Sp.)
- Singh, I. & Singh I. (633) (Bl.)  
— with Singh, (635) (Bl.)
- Skrimnik A. N. with Pavlovskii 223 (R.F.)
- Sladden R. A. with Macgrath, Adams  
King Totter & Rigby 821 (Mal.)
- Sloan, N. R. 460 (1163) (Lep.)
- Sloan T. B. M. 655 (Lep.)
- Smadel J. E. Rights F. L. & Jackson E. B.  
547 919 (Typh.)
- Smart G. A. & Daley R. 1160 (Sp.)
- Smart J. 494 (Ent.)
- Smith, A. & Groves, D. P., 965 (Ent.)
- Smith C. S. with Knowles 710 (Mal.)
- Smith, C. N. & Gouck H. K. (494) 1193  
(Ent.)
- Smith D. T. with Weeks, 654 (Lep.)
- Smith F. with Donovick & Farrell, 635  
(Typh.)
- Smith, G. E. with Metcalf, Hess Jeffery &  
Ludwig 102 (Mal.)
- Smith, H. M. (954) (Am.)
- Smith, L. A. 440 (Dys.)
- Smith, L. H. & Stoeckle J. D. 1109 (Mal.)
- Smith, P. K. 1131 (Typh.)
- Smith, R. E. Stormont R. T. Bianco A. A.  
& Evans R. L. (1157) (Hel.)
- Smith, R. L., 281 (Mal.)
- Smithburn K. C. 214 (Y.F.) 859 (Misc. Dis.)  
— & Mahaffy A. F. 34 (Y.F.)
- Smyth M. J. 1140 (Am.)
- Sneddon, I. B. with Clarke 944 1059 (Def.  
Dis.)  
(423)
- Snell A. M. 1039 (Am.)
- Snyder F. M. & Morton F. A. 1196 (Ent.)
- Snyder J. C. with Ecke Gilliam Yeomans  
Zarafonitis & Murray 545 (Typh.)
- with Murray & Zarafonitis 433 (Typh.)
- with Yeomans & Gilliam 24 (Typh.)
- with — Murray Ecke & Zarafonitis  
636 (Typh.)
- & Zarafonitis C. J. D. 433 (Typh.)
- with — Ecke Yeomans & Murray  
912 (Typh.)
- — & Liu W. T. 426 (Typh.)
- with — & Murray 922 (Typh.)
- Sobrinho O. P. 775 (Am.)
- with Vernani & Martins 754 (Hel.)
- Sodeman W. A. & Lewis B. O. 135 (Am.)
- Sofia F. & Caravino E. 37 (Am.)
- Sofiev M. S. & Leonova, N. A. 744 (R.F.)
- Sokoloff B. 557 (Am.)
- Sokolow M. & Garland L. H. 432 (Typh.)
- Sollmann T. with Luckiesh, Taylor & Cole  
675 (Heat Str.)
- Soman D. W. & Nal S. K. 439 (CHI.)
- Somers, R. B. U. 327 (Typh.)
- Somervell T. H. 1040 (Am.)
- Sommer H. E. with Freund Thomson  
Walter & Schenkeln 311 (Mal.)
- with — & Walter 311 (Mal.)
- Sompayrac L. & Spence H. (1145) (Y.s.)
- Sonneborn D. G. 583 (Vms.)
- Soto C. M. with Fernández 850 (Lep.)
- Soto H. 815 (Mal.)
- with Hoffaker & Rey 392 (Mal.)
- with Rev & Hoffaker (816) (Mal.)
- Sotolouga, F. Alfonso J. & Del Valle  
Aleman S. (50) (Hel.)
- Soule W. H. with Lofgren, 535 (446) (R.F.)
- South Africa, Union of 899 (Mal.)
- de Souza Araújo H. C. 655 (Lep.)
- South African Med. J. 498 *ter* (Reports etc.)
- South African Red Cross Society (Natal  
Branch) 665 (Def. Dis.)
- Souza, P. R. with Campos 47 (Lep.)
- Spadaro O. 41 (Am.)
- Sparkman R. E. with Kiker 303 (Mal.)
- Speck, J. F. Moulder J. W. & Evans E. A.  
Jr. 1116 (Mal.)
- Spector H. & Hamilton T. S. (378) (Heat  
Str.)
- — & Mitchell H. H. 591 (Heat Str.)
- Mitchell, H. H. & Hamilton T. S.  
(378) 591 (Heat Str.)
- Spector S. Haviland J. W. & Coggeshall  
L. T. 823 (Mal.)
- Spence H. with Sompayrac (1145) (Y.s.)
- Spencer G. J. 865 (Lab.)
- Spicer S. S. 282 (Mal.)
- Spies T. D. 582 771 (Haem.)
- Frommeyer W. B. Garcia Lopez G.  
Lopez Toca, R. & Gwiner G. 949 (Sp.)
- Lopez G. G. Menéndez J. A. Minnich  
& Koch, M. B. 474 (Sp.)
- Milanes F. Menéndez, A. Koch M. B.  
& Minnich, V. 769 (Sp.)
- & Morey M. M. 763 (Def. Dis.)
- Perry D. J., Cogswell, R. C. & From  
meyer W. B. 60 (Def. Dis.)
- Vilter C. F. Chino J. H. & Frommeyer  
W. B. 772 (Haem.)

Spies T D with Vilter C. F., & Koch, 373  
(Haem)  
— & Caldwell, M. H. 373  
(Haem)  
Spillars } D 944 (Def Ds)  
Sprink A 308 (Mal)  
— & Tittel M M 399 *see* 400 707  
(Mal)  
— & Macgrath B G (707) (Mal)  
pte S with Allen 23 (Typh)  
— with Ash, 691 (B R)  
Sprecher A 849 (Lep)  
Spurger L with Carum (1170) (Der)  
Stager R F with Macle D & Fuller  
Knapp Stenacker Traub Jellison Miles-  
pugh Austrian Bell Koble Wei Han &  
Graham 917 (Typh)  
Stammers F M G & Whitfield F G S 938  
(Ent)  
Stanbury J B & Huch J H (257)  
(Ent)  
Stannus H S 664 (Reports etc)  
Stave F J with Williamson, Hegetad &  
McKibben 1009 (Mal)  
Stefanopoulos G Canbet, P & Duvoion, S  
Mills 417 420 (Tryp)  
— with Laver 463 (Hel)  
Stefanopoulos G J with Rouband &  
Duolon Mills 419 (Tryp)  
Steinacker M L with Macle Davis,  
Fuller Knapp Stager Traub Jellison  
Miles-pugh, Austrian, Bell Koble, Wei Han  
& Graham 917 (Typh)  
Stenale, M L with Lachen 794 (Ent)  
Stella, E (864) (Ent)  
Steins, T with Wharton 1034 (Hel)  
Stemming, J C 483 (Heat Str)  
Stephan, E., (1077) (Misc Ds)  
Steinberg, T H with Dandelle Rein &  
Sheldon 1043 (Is)  
Stevens T S with Fulton 1121 (Tryp)  
Stevenson D S 407 (Mal)  
Stevenson, I P (1164) (Haem)  
Stewart, J L 607 (Tryp)  
Stewart, M O with Flocks Hammon &  
Laurent, 737 (Den)  
— with — & Mugrage 438 (Den)  
Storn D G with van der Walt 900 (Misc  
Ds)  
Storli, H Simmons, S W & Tarrwell C M  
Tid (Ent)  
— with Tarrwell, 791 (Ent)  
Studer W C, Jr with Brown & Bethes, 930  
(Hel)  
Stock F E 1171 (Oph)  
Stock, P G 14 (Y F)  
Stockdale F 70 (Reports etc)  
Storckle, F D with Smith, 1109 (Mal)  
Stokes, J F 299 (Mal)  
Stone A 6 (Mal)  
Stonham, F V 705 (Mal)  
Stormont, R T with Smith, Hamco &  
E ans, (1157) (Hel)  
Stowman, K 123 (Chl)  
Stratman Thomas W K with Knatch,  
Ellot & Boock, 1113 (Mal)  
Stringer A with Page & Blackith, 600  
(Ent)  
Stuart B M & Pullen, R L 836 (Typh)

Stuart G 44 (R F)  
Stubbs, R E. with Moyns Crowdy Citrine,  
MacKinnon, Blacklock, Engledow &  
Henderson, 70 (Reports etc)  
Stubbs T H with Boyd & Weinstein, 1200  
(Reports, etc)  
— with Moore Young & Hardman, 1002  
(Mal)  
— with Young, Moore Ehrman Hardman,  
Ellis & Burgess 5 (Mal)  
Stubenbord, W D 1045 (Is)  
— & Allen, R F 1050 (Hel)  
Stuhmer A 123 (Typh)  
Sukres R M Diaz Rivera, R S. & Hernandez  
Morales F 496 (Lab)  
— & Hernandez Morales F., 349 (Hel)  
Subbarow Y with Little 533 (Tryp)  
Subramaniam R 457 (Lep) (852) (Hel)  
Suessenguth H & Khoo, R S 360 (Hel)  
Sullivan R. R with Philip & Woodward  
733 (Typh)  
Sullivan J de S with Davis 1026 (Tryp)  
Sulzberger M B Addenbrooke E F., Joyce  
S J Greenberg, S & Mack A G 1166  
(Der)  
Summers, W A with Harris 560 (Hel)  
Sunderly with Wain, (487) (Der)  
Surova, B 323 (Typh)  
— with Grund (324) (Typh)  
— with Martin, Le Roy Babouot &  
Bourcart, 464 (Hel)  
Swanson, E with Fay 781 (Heat Str)  
Suth W D & Antonio Echandi, G R  
(1037) (Hel)  
Swaroop S with Jacob 74 (Reports etc)  
235 (Mal)  
Swartz, W B & Wanamaker J F 906 (Ent)  
Swaney J S Friedlander R D & Queen,  
F B 114 (Leish)  
Sweetman H L 1194 (1195) (Ent)  
Sweilengibel, N H & Schuffner W A. P.,  
(335) (Hel)  
— with ander huyp E 267 (B R)  
Sylla A 114 (Typh)

## T

Taft, W C & Pike J B 447 (R F)  
Tamura, J A Bonagima, R C. & Niso F  
487 (Der)  
Talaferro L G with Talaferro & Simmons,  
629 (Mal)  
Talaferro, W H 414 (Mal)  
— & Bloom, W 630 (Mal)  
— Talaferro L G & Simmons E. L.  
629 (Mal)  
Tahoe R 692 (B R)  
Tahoe R V 112 (Tryp)  
— & Lopez Fernandez J 112 (Tryp)  
— & MacKinnon, J E 292 (Mal)  
Tan C C & Lin, Y., 333 (Am)  
Tang, L L with Chen & Wang, (87) (Mal)  
Tanganyika Territory 79 (Reports, etc.)  
Tarnoky A L with King & Gukhrat, (707)  
(Mal)  
Tarr L 657 (Hel)  
Tarrwell C M. & Storch H 791 (Ent)  
— with — & Simmons, 792 (Ent)

- Tattersall R. V. 28 (Typh.)  
 — & Parry T. E. 430 (Typh.)  
 Taylor A. H. with Luckiesh Colo. & Sollmann, 675 (Heat Str.)  
 Taylor C. E. 342 (Lep.) 596 (Misc. Dis.)  
 Taylor J. 317 (Leish.)  
 Taylor R. V. with Waddell 33 (Y. F.)  
 Tchernomoretz I. 539 (Leish.)  
 — with Adler & Ber. 114 (Leish.)  
 Telcelra, Q. de A. 77 (Reports etc.)  
 Tenen M. M. with Iams & Flanagan 587 (Der.)  
 Tennent, D. M. with Edison & Silber 363 (Def. Dis.)  
 Terracini, E. with Romafia 110 (110) (Tryp.)  
 Thangavolu M. with Reddy 495 (Lab.)  
 van Thiel P. H. with Luen 719 (Tryp.)  
 Thomas C. with Drouet Herbeval & Faivre 467 (Hel.)  
 Thomas, C. R. 195 (Rab.)  
 Thompson A. W. S. 709 (Mal.)  
 Thompson C. M. with McDannel & White 1060 (Def. Dis.)  
 Thompson J. H. 98 (Mal.)  
 — with Rifkin 353 (Hel.)  
 Thompson K. J. Rifkin & Zarrow M. 468 (Hel.)  
 Thomson V. with Larsen 1194 (Ent.)  
 Thomson K. J. with Freund Sommer Walter & Schenckeln, 311 (Mal.)  
 Thomson R. C. M. 93 (Mal.)  
 Thonard Neumann E. 520 (Mal.)  
 Tierney N. A. 920 (Typh.)  
 Tilden, I. L. 455 (Lep.)  
 — with Arnold 452 (Lep.)  
 Tinkham E. R. 671 (Vms.)  
 Tissot J. (355) (Hel.)  
 Titman, W. L. with Cullinan Kekwick & Watts, 942 (Def. Dis.)  
 Todd A. R. with Hull, Lovell Openshaw & Payman (822) (Mal.)  
 Toledo S. de A. (1182) (Oph.)  
 Tomlinson, W. J. 378 (Haem.)  
 Tompsett, R. R. & Kauer G. L. 45 (Ys.)  
 Tonkin J. M. & Work, T. S. 1012 (Mal.)  
 Tong That-Tung with Meyer May Ho-Dac Di, Vu Dinh Tung & Dinh Van Thang 87 (B.R.)  
 Toomey A. G. 1006 (Mal.)  
 Topping, N. H. 20 bis 31 212 (Typh.)  
 — Bengtson I. A. & Henderson R. G. 20 (Typh.)  
 — with — & — 19 (Typh.)  
 — — & Shear M. J. 18 (Typh.)  
 — with Henderson 20 (Typh.)  
 — — & Bengtson I. A. 21 (Typh.)  
 — with Irons Shepard & Cox 924 (Typh.)  
 — & Shepard C. C. 910 911 (Typh.)  
 — with — 21 735 (Typh.)  
 Torrealba F. J. 831 (Tryp.)  
 — with Dias 109 (Tryp.)  
 Torres C. M. & Pinto C. 658 1158 (Hel.)  
 Tottet, M. M., with Macgrath Adams King Rugby & Sladden 821 (Mal.)  
 — with Spinks 398 bis 400 707 (Mal.)  
 — with — & Macgrath, (707) (Mal.)  
 Toullec F. (595) (Misc. Dis.)  
 Tournanoff C. 873 (B.R.)  
 Townshend R. H. with Adams & King 400 (Mal.)  
 — with — Macgrath King, Davey & Havard 402 (Mal.)  
 — with Macgrath, Adams King, Davey & Havard 402 (Mal.)  
 Trager W. Bang F. B. & Haurston, V. G. 821 (Mal.)  
 Traub R. with Mackie Davis Fuller Knapp Steenacker Stager Jellison Millsbaugh, Austrian Bell Kohls Wei Hsi & Graham 917 (Typh.)  
 Travassos J. & Vallejo-Freire A. 642 (Typh.)  
 Travis B. V. with Gahan & Lindquist, 99 (Mal.)  
 — with — Morton & Lindquist 99 (Mal.)  
 — with Lindquist, Madden & Human 795 (Ent.)  
 — with — Schroeder & Jones 159 (Ent.)  
 Tredway J. B. with Harvey & Kuffler 490 (Misc. Dis.)  
 Trembley H. L. with Coatsney & Cooper 629 (Mal.)  
 Trenchard H. J. 1073 (Misc. Dis.)  
 Trespalacios F. & Gonzalez Pineda M. A. 934 (Lep.)  
 Trim A. R. with Alexander 569 (Hel.)  
 Trinder P. with Black & Fourman 667 1161 (Sp.)  
 Troitsky N. V. 745 bis (R.F.)  
 Trout, C. L. 341 (Lep.)  
 Trowell H. C. 684 (Reports etc.) 1062 (Def. Dis.)  
 — & Muiwan E. M. K. 143 363 (Def. Dis.)  
 Truesdell M. with Johnson & Jahn, 67 (Prot.)  
 Truesdell R. E. & Johnson G., (254) (Prot.)  
 Trypanosomiasis Committee of Southern Rhodesia, 907 (Tryp.)  
 Tshumakov P. P. 1077 (Ent.)  
 Tsuchiya H. 332 (Am.)  
 — & Kenamore B. 743 (Am.)  
 Tubangu M. A. 832 (Hel.)  
 Tucker H. A. 1158 (Hel.)  
 — with Keen 1189 (Misc. Dis.)  
 — with — & Miller 597 (Misc. Dis.)  
 Tucker W. A. L. 561 (R.F.)  
 Tuoy G. A. P. (822) (Mal.)  
 — with Card Davis, Onen & Rose (1110) (Mal.)  
 Tumulty P. A. Nichols E. Singewald M. L. & Lutz, T. 819 (Mal.)  
 Tupikova N. A. with Gellhorn, van Dyke & Pyles 722 (Leish.)  
 Tupunambá, A. A. with Martins & Versiani, 718 bis (Tryp.)  
 Turner, E. L. with Bent, Holloway & Cuff 253 (Misc. Dis.)  
 Twining H. E. Dixon H. M. & Weedman F. D. 874 (Der.)  
 Tye M. 588 (Misc. Dis.)



- Consworth, K. with Bertram & Gordon 1197 (Ent.)  
 — & Gordon R. M. 1195 (Ent.)  
 Uetz O. with Janssen, (1905) (Mal.)  
 Upholt W. M. with Arnold & Ferguson '73 (Ent.)  
 — (Gaines T. B. Simmons S. W. & Arnold F. H. '74 (Ent.)  
 Upton R. G. 649 (Pl.)

## V

- Vaquer J. M. 854 (Misc. Dis.)  
 Vallejo-Freire, A. with Travassos 642 (Typh.)  
 van den Bergh, L. 491 (Misc. Dis.)  
 van den Ende M. with Buckland, Dodgson, Edward Henderson-Begg, MacCallum, Veen & Rowlands with Bergmann, Curtis & Shepherd, 436 (Typh.)  
 — Locket & Hargreaves W. H. Viers J. & Lennhoff L. 918 (Typh.)  
 Van der Kamp E. with Swellengrebel 307 (B.R.)  
 Vanderplank, F. L. 494 (Ent.)  
 Van der Sar A. 891 (Misc. Dis.)  
 Vanderechere J. with Wolfe Clancy & Cox 735 (Typh.)  
 Van der Walt b. J. & Steyn D. G. 890 (Misc. Dis.)  
 Vasm, V. 284 (B.R.)  
 Vasey A. with Hullemund Debra & Duguet 635 (Hel.)  
 Varela, G. 672 (Der.)  
 — with Bostamante & Ortiz Marnotte 1134 (Typh.)  
 — with Marnotte 1135 (Typh.)  
 Varpa, L. 905 (Mal.)  
 Varley F. M. & Weldon P. R. 210 (Typh.)  
 Varadon, X. B. with Rydson 630 (Mal.)  
 Varol, 803 (Reports etc.)  
 Vargha, A. M. Flower J. W. & Shropshire G. (157) (Misc. Dis.)  
 Veenraghavan, N. 194 (Rab.)  
 Vetha, G. D. with Menon, (297) (Mal.)  
 Veenag W. L. with Harrell Wolf & Rembert, 823 (Typh.)  
 Verloorn, F. with Homig 884 (B.R.)  
 Vervani, V. with Martins, (904) (Mal.)  
 — & Sobrinho O. P. 754 (Hel.)  
 — with — & Tepuzamba, 713 & (Typh.)  
 Viel B. & Romero H. 845 (Typh.)  
 Villanueva, A. with Martinez Barz, 747 (R.F.)  
 de Villiers V. M. 495 (Reports, etc.)  
 Vilter C. F. with Blankenhorn Schenker & Austin 945 (Def. Dis.)  
 — with Spoon, Chme & Froemeyer 772 (Haem.)  
 — & Koch, M. B. 378 (Haem.)  
 — with — & Caldwell, 375 (Haem.)  
 Vincent H. 250 (Ulc.)  
 Vincke I. with Parent, M. 307 (Mal.)  
 — Bertaux, M. & de Meulenaere J. 291 (Mal.)  
 Viole H. & Calamot, L. (730) (Typh.)  
 Vishnovskaya, S. M., 865 (Hel.)

## W

- Vivranathan, D. K. 285 (Mal.)  
 Vivranathan R., 232 (Misc. Dis.)  
 Vitimskaya I. A. with Leitman 1143 (Am.)  
 Viscarrondo R. O. 719 (Typh.)  
 Volmer H. & Laebig H. 201 (Mal.)  
 Vos J. J. T. with Brug, 33\* (Prot.)  
 Vu Dinh-Tung, with Meyer May Ho-Dac Di, Tong That Tung & Dinh-Van-Thang 87 (B.R.)
- Waddell M. B. 714 (N.F.)  
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